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(54) Title: MOLECULES FOR DISEASE DETECTION AND TREATMENT

(57) Abstract: Various embodiments of the invention provide human molecules for disease detection and treatment (MDDT) and polynucleotides which identify and encode MDDT. Embodiments of the invention also provide expression vectors, host cells, antibodies, agonists, and antagonists. Other embodiments provide methods for diagnosing, treating, or preventing disorders associated with aberrant expression of MDDT.

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## MOLECULES FOR DISEASE DETECTION AND TREATMENT

### TECHNICAL FIELD

The invention relates to novel nucleic acids, molecules for disease detection and treatment encoded by these nucleic acids, and to the use of these nucleic acids and proteins in the diagnosis, treatment, and prevention of cell proliferative, autoimmune/inflammatory, developmental, and neurological disorders, diseases treated with steroids and disorders caused by the metabolic response to treatment with steroids. The invention also relates to the assessment of the effects of exogenous compounds on the expression of nucleic acids and molecules for disease detection and treatment.

### BACKGROUND OF THE INVENTION

It is estimated that only 2% of mammalian DNA encodes proteins, and only a small fraction of the genes that encode proteins are actually expressed in a particular cell at any time. The various types of cells in a multicellular organism differ dramatically both in structure and function, and the identity of a particular cell is conferred by its unique pattern of gene expression. In addition, different cell types express overlapping but distinctive sets of genes throughout development. Cell growth and proliferation, cell differentiation, the immune response, apoptosis, and other processes that contribute to organismal development and survival are governed by regulation of gene expression. An example of a mammalian apoptosis-associated protein is Diablo, which can bind to apoptosis inhibition proteins and antagonize their antiapoptotic effect, a function analogous to that of the proapoptotic *Drosophila* molecules, Grim, Reaper, and HID (Ekert, P.G. et al. (2001) *J. Cell Biol.* 152:483-90). Appropriate gene regulation also ensures that cells function efficiently by expressing only those genes whose functions are required at a given time. Factors that influence gene expression include extracellular signals that mediate cell-cell communication and coordinate the activities of different cell types. Gene expression is regulated at the level of DNA and RNA transcription, and at the level of mRNA translation.

Aberrant expression or mutations in genes and their products may cause, or increase susceptibility to, a variety of human diseases such as cancer and other cell proliferative disorders. The identification of these genes and their products is the basis of an ever-expanding effort to find markers for early detection of diseases and targets for their prevention and treatment. For example, cancer represents a type of cell proliferative disorder that affects nearly every tissue in the body. The development of cancer, or oncogenesis, is often correlated with the conversion of a normal gene into a cancer-causing gene, or oncogene, through abnormal expression or mutation. Oncoproteins, the products of oncogenes, include a variety of molecules that influence cell proliferation, such as growth factors, growth factor receptors, intracellular signal transducers, nuclear transcription factors, and

cell-cycle control proteins. In contrast, tumor-suppressor genes are involved in inhibiting cell proliferation. Mutations which reduce or abrogate the function of tumor-suppressor genes result in aberrant cell proliferation and cancer. Thus a wide variety of genes and their products have been found that are associated with cell proliferative disorders such as cancer, but many more may exist  
5 that are yet to be discovered.

DNA-based arrays can provide an efficient, high-throughput method to examine gene expression and genetic variability. For example, SNPs, or single nucleotide polymorphisms, are the most common type of human genetic variation. DNA-based arrays can dramatically accelerate the discovery of SNPs in hundreds and even thousands of genes. Likewise, such arrays can be used for  
10 SNP genotyping in which DNA samples from individuals or populations are assayed for the presence of selected SNPs. These approaches will ultimately lead to the systematic identification of all genetic variations in the human genome and the correlation of certain genetic variations with disease susceptibility, responsiveness to drug treatments, and other medically relevant information. (See, for example, Wang, D.G. et al. (1998) Science 280:1077-1082.)

DNA-based arrays can also provide a simple way to explore the expression of a single polymorphic gene. When the expression of a single gene is explored, DNA-based arrays are employed to detect the expression of specific gene variants. For example, a p53 tumor suppressor gene array is used to determine whether individuals are carrying mutations that predispose them to cancer. A cytochrome p450 gene array is useful to determine whether individuals have one of a  
20 number of specific mutations that could result in increased drug metabolism, drug resistance or drug toxicity.

DNA-based array technology is especially important for the rapid analysis of global gene expression patterns. There is a growing awareness that gene expression is affected in a global fashion. In some cases the interactions may be expected, such as when the genes are part of the same  
25 signaling pathway. In other cases, such as when the genes participate in separate signaling pathways, the interactions may be totally unexpected. Therefore, DNA-based arrays can be used to investigate how genetic predisposition, disease, or therapeutic treatment affects the expression of a large number of genes. In this case, it is useful to develop a profile, or transcript image, of all the genes that are expressed and the levels at which they are expressed in that particular tissue. A profile generated  
30 from an individual or population affected with a certain disease or undergoing a particular therapy may be compared with a profile generated from a control individual or population. Such analysis does not require knowledge of gene function, as the expression profiles can be subjected to mathematical analyses which simply treat each gene as a marker. Furthermore, gene expression profiles may help dissect biological pathways by identifying all the genes expressed, for example, at a  
35 certain developmental stage, in a particular tissue, or in response to disease or treatment. (See, for



example, Lander, E.S. et al. (1996) Science 274:536-539.)

Certain genes are known to be associated with diseases because of their chromosomal location, such as the genes in the myotonic dystrophy (DM) regions of mouse and human. The mutation underlying DM has been localized to a gene encoding the DM-kinase protein, but another active gene, DMR-N9, is in close proximity to the DM-kinase gene (Jansen, G. et al. (1992) Nat. Genet. 1:261-266). DMR-N9 encodes a 650 amino acid protein that contains WD repeats, motifs found in cell signaling proteins. DMR-N9 is expressed in all neural tissues and in the testis, suggesting a role for DMR-N9 in the manifestation of mental and testicular symptoms in severe cases of DM (Jansen, G. et al. (1995) Hum. Mol. Genet. 4:843-852).

Other genes are identified based upon their expression patterns or association with disease syndromes. For example, autoantibodies to subcellular organelles are found in patients with systemic rheumatic diseases. A recently identified protein, golgin-67, belongs to a family of Golgi autoantigens having alpha-helical coiled-coil domains (Eystathioy, T. et al. (2000) J. Autoimmun. 14:179-187). The Stac gene was identified as a brain specific, developmentally regulated gene. The Stac protein contains an SH3 domain, and is thought to be involved in neuron-specific signal transduction (Suzuki, H. et al. (1996) Biochem. Biophys. Res. Commun. 229:902-909).

Evi-5 is a site of retroviral integration in AKXD T-cell lymphoma cells. Tumors with Evi-5 integrations have also been shown to possess other integration sites associated with T-cell disease. Retroviral disease induction occurs as a result of insertional mutagenesis of cellular proto-oncogenes or tumor suppressor genes. The AKXD recombinant inbred murine model is useful in the study of retrovirally-induced myeloid tumors, as well as T- and B-cell leukemias (Liao, X. et al. (1997) Oncogene 14:1023-1029). Lymphomas with integrations in Evi-5 may also possess integrations in *Myc*, in sites located near and activating *Myc*, or that synergize with *Myc*. This suggests a possible cooperation between Evi-5 with *Myc* in tumor induction, consistent with other observations showing that *Myc* is a frequent target of retroviral integration in mouse and rat T-cell lymphomas.

The contiguous gene deletion syndrome AMME is characterized by Alport syndrome, midface hypoplasia, mental retardation and elliptocytosis and is caused by a deletion in Xq22.3, comprising several genes including COL4A5, FACIL4 and AMMECR1. AMMECR1, found in eukaryotic and prokaryotic cells, contains six exons and codes for a protein with a molecular mass of 35.5 kDa. Evidence suggests that this protein is a regulatory factor potentially involved in the development of AMME contiguous gene deletion syndrome. The mouse ortholog has 95.2% identity at the amino acid level with human AMMECR1 and maps to chromosome MmuXF1-F3 (Vitelli, F. et al. (1999) Genomics 55:335-340; Vitelli, F. et al. (2000) Cytogenet. Cell Genet. 88:259-263).

Sporulation-induced transcript 4 (SIT4) gene is a type 2A-related serine/threonine protein phosphatase which when overexpressed confers lithium tolerance in galactose medium to the budding

yeast, *Saccharomyces cerevisiae*. It is a regulator of the cell cycle and is involved in nitrogen sensing, normal g1 cyclin expression, and bud initiation (Masuda, C. A. et al. (2000) J. Biol. Chem. 275:30957-30961). The SIT4-associated proteins (SAPs), SAP155, SAP185, SAP190, and probably SAP4, associate with SIT4 in separate complexes. The SAPs are not functional in the absence of SIT4 and likewise, SIT4 is not functional in the absence of the SAPs. However, SAPs and SIT4 have distinct functions (Luke, M. M. et al. (1996) Mol. Cell. Biol. 16:2744-2755). C11orf23 is a human ortholog of the yeast SAP family. C11orf23 has been mapped to the 400-kb region of the IDDM4 locus of chromosome 11q13, a region involved in type 1 diabetes (Twells, R. C. et al. (2001) Genomics 72:231-242).

Dendritic cells are antigen-presenting cells that play a major role in the initial phases of the immune response. Dendritic cells located in peripheral tissues are generally immature and exhibit a strong capacity to capture surrounding antigens whereas they exhibit limited T cell activation capacity. Reciprocally, mature dendritic cells found in lymphoid organs exhibit a strong capacity to activate T cells but have lost most of their ability to pick up new antigens. Dendritic cells migrating out of transplanted organ play a major role in the induction of graft rejection. Therefore, genes that are modulated during the maturation of dendritic cells represent potential targets for drugs aimed at limiting the rejection of transplanted organs.

Rho-family GTPases are critical mediators of dendritic growth and remodeling. Three of these Rho GTPases, RhoA, Rac1 and Cdc42 (cell division cycle 42), regulate distinct aspects of dendritic development, such as dendrite initiation, dendrite growth, dendrite branching, and spine formation. In cortical neurons, Rho-family GTPases play a central role in determining the number of primary dendrites in both pyramidal and non-pyramidal neurons. Research suggests that Rac1 is an important effector of dendrite initiation and that a common effector of Rac1 and Cdc42 mediates dendrite initiation. Suggested effectors include the p21-activated kinase (PAK) family of serine threonine kinases and LIM-domain-containing protein kinase, which can modulate actin dynamics by phosphorylation of cofilin.

Rho-family GTPases also can influence large-scale dendritic remodeling. Many neurons in the cortex initially acquire a pyramidal morphology and undergo a developmentally-regulated transformation into non-pyramidal neurons. This transformation involves the withdrawal of the apical dendrite and the extension of new primary dendrites, and is inhibited by expression of dominant-negative Cdc42 and, to a lesser extent, by dominant-negative Rac1. This inhibition suggests that the acquisition of cell-type-specific dendritic morphologies is under the control of Rac1 and Cdc42 signaling Redmond, L. and Ghosh, A. (2001) Curr. Opin. Neurobiol. 11:111-117).

ADP-ribosylation factors (ARFs) are small guanine-nucleotide-binding proteins that regulate membrane traffic and organelle structure in eukaryotic cells. In general, the inactive GDP-bound

form of ARF is soluble, although it can associate weakly with membranes, whereas the active GTP-bound form binds tightly to the membrane. ARFs function on membrane surfaces where they encounter their effectors and regulators, the guanine nucleotide exchange factors (GEFs) and GTPase-activating proteins (GAPs). ARF effectors include lipid-modifying enzymes and cytosolic coat complexes (such as COPI) that are recruited onto membranes by ARF-GTP. Hence, ARF activation leads to changes in both the lipid and protein composition of the membrane on which it is localized; changes which in turn result in modulation of membrane structure and function.

ARF proteins are highly conserved and have been found in all eukaryotic organisms examined. Mammalian ARF proteins are divided into three classes: Class I (ARF1–ARF3), Class II (ARF4 and ARF5) and Class III (ARF6). Class I ARFs are involved in trafficking in the ER–Golgi and endosomal systems, and their functions have been extensively studied. ARF1 binding to endosomal membranes is regulated by endosomal pH, which explains the pH dependence of COPI binding to endosomes. The Class III ARF, ARF6, functions exclusively in the endosomal–plasma membrane system. ARF6 is involved in endosomal recycling to the plasma membrane (PM), in regulated secretion, and in coordinating actin cytoskeleton changes at the PM. ARF6 is present at the apical surface of Madin Darby Canine Kidney (MDCK) epithelial cells, where it plays a role in modulating clathrin endocytosis. ARF6 has also been implicated in Fc-mediated phagocytosis in macrophages and in insulin stimulation of adipon secretion and Glut4 translocation. By contrast, virtually nothing is known about the functions of the class II ARFs (Donaldson, J. D. and Jackson, C. L. (2000) *Curr. Opin. Cell Biol.* 12:475-482).

#### Expression profiling

Microarrays are analytical tools used in bioanalysis. A microarray has a plurality of molecules spatially distributed over, and stably associated with, the surface of a solid support. Microarrays of polypeptides, polynucleotides, and/or antibodies have been developed and find use in a variety of applications, such as gene sequencing, monitoring gene expression, gene mapping, bacterial identification, drug discovery, and combinatorial chemistry.

One area in particular in which microarrays find use is in gene expression analysis. Array technology can provide a simple way to explore the expression of a single polymorphic gene or the expression profile of a large number of related or unrelated genes. When the expression of a single gene is examined, arrays are employed to detect the expression of a specific gene or its variants. When an expression profile is examined, arrays provide a platform for identifying genes that are tissue specific, are affected by a substance being tested in a toxicology assay, are part of a signaling cascade, carry out housekeeping functions, or are specifically related to a particular genetic predisposition, condition, disease, or disorder.

The potential application of gene expression profiling is particularly relevant to improving

diagnosis, prognosis, and treatment of disease. For example, both the levels and sequences expressed in tissues from subjects with a cardiovascular disorder may be compared with the levels and sequences expressed in normal tissue.

Atherosclerosis and the associated coronary artery disease and cerebral stroke represent the most common cause of death in industrialized nations. Although certain key risk factors have been identified, a full molecular characterization that elucidates the causes and provides care for this complex disease has not been achieved. Molecular characterization of growth and regression of atherosclerotic vascular lesions requires identification of the genes that contribute to features of the lesion including growth, stability, dissolution, rupture and, most lethally, induction of occlusive vessel thrombus. Vascular lesions principally involve the vascular endothelium and the surrounding smooth muscle tissue.

Development of atherosclerosis is understood to be induced by the presence of circulating lipoprotein. Lipoproteins, such as the cholesterol-rich low-density lipoprotein (LDL), accumulate in the extracellular space of the vascular intima, and undergo modification. Oxidation of LDL (Ox-LDL) occurs most avidly in the sub-endothelial space where circulating antioxidant defenses are less effective. Mononuclear phagocytes enter the intima, differentiate into macrophages, and ingest modified lipids including Ox-LDL. During Ox-LDL uptake, macrophages produce cytokines (e.g. tumor necrosis factor  $\alpha$  (TNF- $\alpha$ ) and interleukin-1 (IL-1)) and growth factors (e.g. M-CSF, VEGF, and PDGF-BB) that elicit further cellular events that modulate atherogenesis such as smooth muscle cell proliferation and production of extracellular matrix by vascular endothelium. Additionally, these macrophages may activate genes in endothelium and smooth muscle tissue involved in inflammation and tissue differentiation, including superoxide dismutase (SOD), IL-8, and ICAM-1.

The vascular endothelium influences not only the three classically interacting components of hemostasis: the vessel, the blood platelets and the clotting and fibrinolytic systems of plasma, but also the natural sequelae: inflammation and tissue repair. Two principal modes of endothelial behavior may be differentiated, best defined as an anti- and a prothrombotic state. Under physiological conditions endothelium mediates vascular dilatation (formation of nitric oxide (NO), PGI<sub>2</sub>, adenosine, hyperpolarising factor), prevents platelet adhesion and activation (production of adenosine, NO and PGI<sub>2</sub>, removal of ADP), blocks thrombin formation (tissue factor pathway inhibitor, activation of protein C via thrombomodulin, activation of antithrombin III) and mitigates fibrin deposition (t- and scu plasminogen activator production). Adhesion and transmigration of inflammatory leukocytes are attenuated, e.g. by NO and IL-10, and oxygen radicals are efficiently scavenged (urate, NO, glutathione, SOD).

When the endothelium is physically disrupted or functionally perturbed by postischemic reperfusion, acute and chronic inflammation, atherosclerosis, diabetes and chronic arterial

hypertension, then completely opposing actions pertain. This prothrombotic, proinflammatory state is characterised by vaso-constriction, platelet and leukocyte activation and adhesion (externalization, expression and upregulation of, for example, von Willebrand factor, platelet activating factor, P-selectin, ICAM-1, IL-8, MCP-1, and TNF- $\alpha$ ), promotion of thrombin formation, coagulation and fibrin deposition at the vascular wall (expression of tissue factor, PAI-1, and phosphatidyl serine) and, in platelet-leukocyte coaggregates, additional inflammatory interactions via attachment of platelet CD40-ligand to endothelial, monocyte and B-cell CD40. Since thrombin formation and inflammatory stimulation set the stage for later tissue repair, complete abolition of such endothelial responses cannot be the goal of clinical interventions aimed at limiting procoagulatory, prothrombotic actions of a dysfunctional vascular endothelium. (See, e.g., Becker et al. (2000) *Z Kardiol* 89:160-167.)

Tumor necrosis factor  $\alpha$  is a pleiotropic cytokine that mediates immune regulation and inflammatory responses. TNF- $\alpha$ -related cytokines generate partially overlapping cellular responses, including differentiation, proliferation, nuclear factor- $\kappa$ B (NF- $\kappa$ B) activation, and cell death, by triggering the aggregation of receptor monomers (Smith, C.A. et al. (1994) *Cell* 76:959-962). The cellular responses triggered by TNF- $\alpha$  are initiated through its interaction with distinct cell surface receptors (TNFRs). NF- $\kappa$ B is a transcription factor with a pivotal role in inducing genes involved in physiological processes as well as in the response to injury and infection. Activation of NF- $\kappa$ B involves the phosphorylation and subsequent degradation of an inhibitory protein, I $\kappa$ B, and many of the proximal kinases and adaptor molecules involved in this process have been elucidated. Additionally, the NF- $\kappa$ B activation pathway from cell membrane to nucleus for IL-1 and TNF- $\alpha$  is now understood (Bowie and O'Neill (2000) *Biochem Pharmacol* 59:13-23).

Monocyte chemoattractant protein-1 (MCP-1) is known to play an important role in the pathogenesis of atherosclerosis by inducing monocyte migration. TNF- $\alpha$  treatment of human umbilical vein endothelial cells (HUVECs) increased the cellular secretions of MCP-1 119-fold compared with untreated cells. Troglitazone, an insulin-sensitizing drug, significantly inhibited this TNF- $\alpha$ -induced increase in MCP-1 secretions and decreased mRNA levels (Ohta et al. (2000) *Diabetes Res Clin Pract* 48:171-176).

Treatment of confluent cultures of vascular smooth muscle cells (SMCs) with TNF- $\alpha$  suppresses the incorporation of [ $^3$ H]proline into both collagenase-digestible proteins (CDP) and noncollagenous proteins (NCP). Such suppression by TNF- $\alpha$  is not observed in confluent bovine aortic endothelial cells and human fibroblastic IMR-90 cells. TNF- $\alpha$  decreases the relative proportion of collagen types IV and V suggesting that TNF- $\alpha$  modulates collagen synthesis by SMCs depending on their cell density and therefore may modify formation of atherosclerotic lesions (Hiraga et al. (2000) *Life Sci* 66:235-244).

Human coronary artery smooth muscle cells (CASMC) are primary cells isolated from the tunica media (an intermediate muscular layer) of a human coronary artery. Vascular smooth muscle cells are a model of increasing significance in vascular biology. It is now well known that besides their obvious role in the regulation of vascular tone and, consequently, oxygen supply to various tissues, their behavior under inflammatory conditions is an important factor in the development of atherosclerosis and restenosis.

Human aortic endothelial cells (HAECs) are primary cells derived from the endothelium of a human aorta. HAECs have been used as an experimental model for investigating *in vitro* the role of the endothelium in human vascular biology. Activation of the vascular endothelium is considered to be a central event in a wide range of both physiological and pathophysiological processes, such as vascular tone regulation, coagulation and thrombosis, atherosclerosis, and inflammation.

Thus, vascular tissue genes differentially expressed during treatment of CASMC and HAEC cell cultures with TNF $\alpha$  may reasonably be expected to be markers of the atherosclerotic process.

The potential application of gene expression profiling is particularly relevant to improving diagnosis, prognosis, and treatment of disease. For example, both the levels and sequences expressed in tissues from subjects with ovarian cancer may be compared with the levels and sequences expressed in normal tissue. Ovarian cancer is the leading cause of death from a gynecologic cancer. The majority of ovarian cancers are derived from epithelial cells, and 70% of patients with epithelial ovarian cancers present with late-stage disease. As a result, the long-term survival rate for individuals with this disease is very low. Identification of early-stage markers for ovarian cancer would significantly increase the survival rate. The molecular events that lead to ovarian cancer are poorly understood. Some of the known aberrations include mutation of p53 and microsatellite instability. Since gene expression patterns likely vary when normal ovary is compared to ovarian tumors, examination of gene expression in these tissues can identify possible markers for ovarian cancer.

Steroids are a class of lipid-soluble molecules, including cholesterol, bile acids, vitamin D, and hormones, that share a common four-ring structure based on cyclopentanoperhydrophenanthrene and that carry out a wide variety of functions. Cholesterol, for example, is a component of cell membranes that controls membrane fluidity. It is also a precursor for bile acids which solubilize lipids and facilitate absorption in the small intestine during digestion. Vitamin D regulates the absorption of calcium in the small intestine and controls the concentration of calcium in plasma. Steroid hormones, produced by the adrenal cortex, ovaries, and testes, include glucocorticoids, mineralocorticoids, androgens, and estrogens. They control various biological processes by binding to intracellular receptors that regulate transcription of specific genes in the nucleus. Glucocorticoids, for example, increase blood glucose concentrations by regulation of gluconeogenesis in the liver, increase blood concentrations of fatty acids by promoting lipolysis in adipose tissues, modulate

sensitivity to catecholamines in the central nervous system, and reduce inflammation. The principal mineralocorticoid, aldosterone, is produced by the adrenal cortex and acts on cells of the distal tubules of the kidney to enhance sodium ion reabsorption. Androgens, produced by the interstitial cells of Leydig in the testis, include the male sex hormone testosterone, which triggers changes at puberty, the production of sperm and maintenance of secondary sexual characteristics. Female sex hormones, estrogen and progesterone, are produced by the ovaries and also by the placenta and adrenal cortex of the fetus during pregnancy. Estrogen regulates female reproductive processes and secondary sexual characteristics. Progesterone regulates changes in the endometrium during the menstrual cycle and pregnancy.

Steroid hormones are widely used for fertility control and in anti-inflammatory treatments for physical injuries and diseases such as arthritis, asthma, and auto-immune disorders. Progesterone, a naturally occurring progestin, is primarily used to treat amenorrhea, abnormal uterine bleeding, or as a contraceptive. Endogenous progesterone is responsible for inducing secretory activity in the endometrium of the estrogen-primed uterus in preparation for the implantation of a fertilized egg and for the maintenance of pregnancy. It is secreted from the corpus luteum in response to luteinizing hormone (LH). The primary contraceptive effect of exogenous progestins involves the suppression of the midcycle surge of LH. At the cellular level, progestins diffuse freely into target cells and bind to the progesterone receptor. Target cells include the female reproductive tract, the mammary gland, the hypothalamus, and the pituitary. Once bound to the receptor, progestins slow the frequency of release of gonadotropin releasing hormone from the hypothalamus and blunt the pre-ovulatory LH surge, thereby preventing follicular maturation and ovulation. Progesterone has minimal estrogenic and androgenic activity. Progesterone is metabolized hepatically to pregnanediol and conjugated with glucuronic acid.

Medroxyprogesterone (MAH), also known as 6 $\alpha$ -methyl-17-hydroxyprogesterone, is a synthetic progestin with a pharmacological activity about 15 times greater than progesterone. MAH is used for the treatment of renal and endometrial carcinomas, amenorrhea, abnormal uterine bleeding, and endometriosis associated with hormonal imbalance. MAH has a stimulatory effect on respiratory centers and has been used in cases of low blood oxygenation caused by sleep apnea, chronic obstructive pulmonary disease, or hypercapnia.

Danazol is a synthetic steroid derived from ethinyl testosterone. Danazol indirectly reduces estrogen production by lowering pituitary synthesis of follicle-stimulating hormone and LH. Danazol also binds to sex hormone receptors in target tissues, thereby exhibiting anabolic, antiestrogenic, and weakly androgenic activity. Danazol does not possess any progestogenic activity, and does not suppress normal pituitary release of corticotropin or release of cortisol by the adrenal glands.

Danazol is used in the treatment of endometriosis to relieve pain and inhibit endometrial cell growth.

It is also used to treat fibrocystic breast disease and hereditary angioedema.

Corticosteroids are used to relieve inflammation and to suppress the immune response. They inhibit eosinophil, basophil, and airway epithelial cell function by regulation of cytokines that mediate the inflammatory response. They inhibit leukocyte infiltration at the site of inflammation, interfere in the function of mediators of the inflammatory response, and suppress the humoral immune response. Corticosteroids are used to treat allergies, asthma, arthritis, and skin conditions. Beclomethasone is a synthetic glucocorticoid that is used to treat steroid-dependent asthma, to relieve symptoms associated with allergic or nonallergic (vasomotor) rhinitis, or to prevent recurrent nasal polyps following surgical removal. The anti-inflammatory and vasoconstrictive effects of intranasal beclomethasone are 5000 times greater than those produced by hydrocortisone.

The anti-inflammatory actions of corticosteroids are thought to involve phospholipase A<sub>2</sub> inhibitory proteins, collectively called lipocortins. Lipocortins, in turn, control the biosynthesis of potent mediators of inflammation such as prostaglandins and leukotrienes by inhibiting the release of the precursor molecule arachidonic acid. Proposed mechanisms of action include decreased IgE synthesis, increased number of  $\beta$ -adrenergic receptors on leukocytes, and decreased arachidonic acid metabolism. During an immediate allergic reaction, such as in chronic bronchial asthma, allergens bridge the IgE antibodies on the surface of mast cells, which triggers these cells to release chemotactic substances. Mast cell influx and activation, therefore, is partially responsible for the inflammation and hyperirritability of the oral mucosa in asthmatic patients. This inflammation can be retarded by administration of corticosteroids. ~~ENDFIELD~~

The potential application of gene expression profiling is particularly relevant to measuring the toxic response to potential therapeutic compounds and the metabolic response to therapeutic agents. Diseases treated with steroids and disorders caused by the metabolic response to treatment with steroids include adenomatosis, cholestasis, cirrhosis, hemangioma, Henoch-Schonlein purpura, hepatitis, hepatocellular and metastatic carcinomas, idiopathic thrombocytopenic purpura, porphyria, sarcoidosis, and Wilson disease. Response may be measured by comparing both the levels and sequences expressed in tissues from subjects exposed to or treated with steroid compounds such as medroxyprogesterone (MAH) or budesonide (bude) with the levels and sequences expressed in normal untreated tissue.

The effects upon liver metabolism and hormone clearance mechanisms are important to understand the pharmacodynamics of a drug. The human C3A cell line is a clonal derivative of HepG2/C3 (hepatoma cell line, isolated from a 15-year-old male with liver tumor), which was selected for strong contact inhibition of growth. The use of a clonal population enhances the reproducibility of the cells. C3A cells have many characteristics of primary human hepatocytes in culture: i) expression of insulin receptor and insulin-like growth factor II receptor; ii) secretion of a



high ratio of serum albumin compared with  $\alpha$ -fetoprotein iii) conversion of ammonia to urea and glutamine; iv) metabolism of aromatic amino acids; and v) proliferation in glucose-free and insulin-free medium. The C3A cell line is now well established as an *in vitro* model of the mature human liver (Mickelson et al. (1995) Hepatology 22:866-875; Nagendra et al. (1997) Am J Physiol 5 272:G408-G416).

There is a need in the art for new compositions, including nucleic acids and proteins, for the diagnosis, prevention, and treatment of cell proliferative, autoimmune/inflammatory, developmental, and neurological disorders, diseases treated with steroids and disorders caused by the metabolic response to treatment with steroids.

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### SUMMARY OF THE INVENTION

Various embodiments of the invention provide purified polypeptides, molecules for disease detection and treatment, referred to collectively as "MDDT" and individually as "MDDT-1," "MDDT-2," "MDDT-3," "MDDT-4," "MDDT-5," "MDDT-6," "MDDT-7," "MDDT-8," "MDDT-9," 15 "MDDT-10," "MDDT-11," "MDDT-12," "MDDT-13," "MDDT-14," "MDDT-15," "MDDT-16," "MDDT-17," "MDDT-18," "MDDT-19," "MDDT-20," "MDDT-21," "MDDT-22," "MDDT-23," "MDDT-24," "MDDT-25," "MDDT-26," "MDDT-27," "MDDT-28," "MDDT-29," "MDDT-30," "MDDT-31," "MDDT-32," "MDDT-33," "MDDT-34," "MDDT-35," "MDDT-36," "MDDT-37," "MDDT-38," "MDDT-39," "MDDT-40," "MDDT-41," "MDDT-42," "MDDT-43," "MDDT-44," 20 "MDDT-45," "MDDT-46," "MDDT-47," "MDDT-48," "MDDT-49," "MDDT-50," "MDDT-51," "MDDT-52," "MDDT-53," "MDDT-54," "MDDT-55," and "MDDT-56" and methods for using these proteins and their encoding polynucleotides for the detection, diagnosis, and treatment of diseases and medical conditions. Embodiments also provide methods for utilizing the purified molecules for disease detection and treatment and/or their encoding polynucleotides for facilitating the drug 25 discovery process, including determination of efficacy, dosage, toxicity, and pharmacology. Related embodiments provide methods for utilizing the purified molecules for disease detection and treatment and/or their encoding polynucleotides for investigating the pathogenesis of diseases and medical conditions.

An embodiment provides an isolated polypeptide selected from the group consisting of a) a 30 polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:1-56, b) a polypeptide comprising a naturally occurring amino acid sequence at least 90% identical or at least about 90% identical to an amino acid sequence selected from the group consisting of SEQ ID NO:1-56, c) a biologically active fragment of a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1-56, and d) an immunogenic fragment of a polypeptide 35 having an amino acid sequence selected from the group consisting of SEQ ID NO:1-56. Another

embodiment provides an isolated polypeptide comprising an amino acid sequence of SEQ ID NO:1-56.

Still another embodiment provides an isolated polynucleotide encoding a polypeptide selected from the group consisting of a) a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:1-56, b) a polypeptide comprising a naturally occurring amino acid sequence at least 90% identical or at least about 90% identical to an amino acid sequence selected from the group consisting of SEQ ID NO:1-56, c) a biologically active fragment of a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1-56, and d) an immunogenic fragment of a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1-56. In another embodiment, the polynucleotide encodes a polypeptide selected from the group consisting of SEQ ID NO:1-56. In an alternative embodiment, the polynucleotide is selected from the group consisting of SEQ ID NO:57-112.

Still another embodiment provides a recombinant polynucleotide comprising a promoter sequence operably linked to a polynucleotide encoding a polypeptide selected from the group consisting of a) a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:1-56, b) a polypeptide comprising a naturally occurring amino acid sequence at least 90% identical or at least about 90% identical to an amino acid sequence selected from the group consisting of SEQ ID NO:1-56, c) a biologically active fragment of a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1-56, and d) an immunogenic fragment of a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1-56. Another embodiment provides a cell transformed with the recombinant polynucleotide. Yet another embodiment provides a transgenic organism comprising the recombinant polynucleotide.

Another embodiment provides a method for producing a polypeptide selected from the group consisting of a) a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:1-56, b) a polypeptide comprising a naturally occurring amino acid sequence at least 90% identical or at least about 90% identical to an amino acid sequence selected from the group consisting of SEQ ID NO:1-56, c) a biologically active fragment of a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1-56, and d) an immunogenic fragment of a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1-56. The method comprises a) culturing a cell under conditions suitable for expression of the polypeptide, wherein said cell is transformed with a recombinant polynucleotide comprising a promoter sequence operably linked to a polynucleotide encoding the polypeptide, and b) recovering the polypeptide so expressed.

Yet another embodiment provides an isolated antibody which specifically binds to a polypeptide selected from the group consisting of a) a polypeptide comprising an amino acid

sequence selected from the group consisting of SEQ ID NO:1-56, b) a polypeptide comprising a naturally occurring amino acid sequence at least 90% identical or at least about 90% identical to an amino acid sequence selected from the group consisting of SEQ ID NO:1-56, c) a biologically active fragment of a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1-56, and d) an immunogenic fragment of a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1-56.

Still yet another embodiment provides an isolated polynucleotide selected from the group consisting of a) a polynucleotide comprising a polynucleotide sequence selected from the group consisting of SEQ ID NO:57-112, b) a polynucleotide comprising a naturally occurring polynucleotide sequence at least 90% identical or at least about 90% identical to a polynucleotide sequence selected from the group consisting of SEQ ID NO:57-112, c) a polynucleotide complementary to the polynucleotide of a), d) a polynucleotide complementary to the polynucleotide of b), and e) an RNA equivalent of a)-d). In other embodiments, the polynucleotide can comprise at least about 20, 30, 40, 60, 80, or 100 contiguous nucleotides.

Yet another embodiment provides a method for detecting a target polynucleotide in a sample, said target polynucleotide being selected from the group consisting of a) a polynucleotide comprising a polynucleotide sequence selected from the group consisting of SEQ ID NO:57-112, b) a polynucleotide comprising a naturally occurring polynucleotide sequence at least 90% identical or at least about 90% identical to a polynucleotide sequence selected from the group consisting of SEQ ID NO:57-112, c) a polynucleotide complementary to the polynucleotide of a), d) a polynucleotide complementary to the polynucleotide of b), and e) an RNA equivalent of a)-d). The method comprises a) hybridizing the sample with a probe comprising at least 20 contiguous nucleotides comprising a sequence complementary to said target polynucleotide in the sample, and which probe specifically hybridizes to said target polynucleotide, under conditions whereby a hybridization complex is formed between said probe and said target polynucleotide or fragments thereof, and b) detecting the presence or absence of said hybridization complex. In a related embodiment, the method can include detecting the amount of the hybridization complex. In still other embodiments, the probe can comprise at least about 20, 30, 40, 60, 80, or 100 contiguous nucleotides.

Still yet another embodiment provides a method for detecting a target polynucleotide in a sample, said target polynucleotide being selected from the group consisting of a) a polynucleotide comprising a polynucleotide sequence selected from the group consisting of SEQ ID NO:57-112, b) a polynucleotide comprising a naturally occurring polynucleotide sequence at least 90% identical or at least about 90% identical to a polynucleotide sequence selected from the group consisting of SEQ ID NO:57-112, c) a polynucleotide complementary to the polynucleotide of a), d) a polynucleotide complementary to the polynucleotide of b), and e) an RNA equivalent of a)-d). The method

comprises a) amplifying said target polynucleotide or fragment thereof using polymerase chain reaction amplification, and b) detecting the presence or absence of said amplified target polynucleotide or fragment thereof. In a related embodiment, the method can include detecting the amount of the amplified target polynucleotide or fragment thereof.

5 Another embodiment provides a composition comprising an effective amount of a polypeptide selected from the group consisting of a) a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:1-56, b) a polypeptide comprising a naturally occurring amino acid sequence at least 90% identical or at least about 90% identical to an amino acid sequence selected from the group consisting of SEQ ID NO:1-56, c) a biologically active  
10 fragment of a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1-56, and d) an immunogenic fragment of a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1-56, and a pharmaceutically acceptable excipient. In one embodiment, the composition can comprise an amino acid sequence selected from the group consisting of SEQ ID NO:1-56. Other embodiments provide a method of treating a disease or  
15 condition associated with decreased or abnormal expression of functional MDDT, comprising administering to a patient in need of such treatment the composition.

Yet another embodiment provides a method for screening a compound for effectiveness as an agonist of a polypeptide selected from the group consisting of a) a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:1-56, b) a polypeptide comprising a  
20 naturally occurring amino acid sequence at least 90% identical or at least about 90% identical to an amino acid sequence selected from the group consisting of SEQ ID NO:1-56, c) a biologically active fragment of a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1-56, and d) an immunogenic fragment of a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1-56. The method comprises a) exposing a sample  
25 comprising the polypeptide to a compound, and b) detecting agonist activity in the sample. Another embodiment provides a composition comprising an agonist compound identified by the method and a pharmaceutically acceptable excipient. Yet another embodiment provides a method of treating a disease or condition associated with decreased expression of functional MDDT, comprising administering to a patient in need of such treatment the composition.

30 Still yet another embodiment provides a method for screening a compound for effectiveness as an antagonist of a polypeptide selected from the group consisting of a) a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:1-56, b) a polypeptide comprising a naturally occurring amino acid sequence at least 90% identical or at least about 90% identical to an amino acid sequence selected from the group consisting of SEQ ID NO:1-56, c) a  
35 biologically active fragment of a polypeptide having an amino acid sequence selected from the group

consisting of SEQ ID NO:1-56, and d) an immunogenic fragment of a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1-56. The method comprises a) exposing a sample comprising the polypeptide to a compound, and b) detecting antagonist activity in the sample. Another embodiment provides a composition comprising an antagonist compound  
5 identified by the method and a pharmaceutically acceptable excipient. Yet another embodiment provides a method of treating a disease or condition associated with overexpression of functional MDDT, comprising administering to a patient in need of such treatment the composition.

Another embodiment provides a method of screening for a compound that specifically binds to a polypeptide selected from the group consisting of a) a polypeptide comprising an amino acid  
10 sequence selected from the group consisting of SEQ ID NO:1-56, b) a polypeptide comprising a naturally occurring amino acid sequence at least 90% identical or at least about 90% identical to an amino acid sequence selected from the group consisting of SEQ ID NO:1-56, c) a biologically active fragment of a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1-56, and d) an immunogenic fragment of a polypeptide having an amino acid sequence  
15 selected from the group consisting of SEQ ID NO:1-56. The method comprises a) combining the polypeptide with at least one test compound under suitable conditions, and b) detecting binding of the polypeptide to the test compound, thereby identifying a compound that specifically binds to the polypeptide.

Yet another embodiment provides a method of screening for a compound that modulates the  
20 activity of a polypeptide selected from the group consisting of a) a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:1-56, b) a polypeptide comprising a naturally occurring amino acid sequence at least 90% identical or at least about 90% identical to an amino acid sequence selected from the group consisting of SEQ ID NO:1-56, c) a biologically active fragment of a polypeptide having an amino acid sequence selected from the group consisting of SEQ  
25 ID NO:1-56, and d) an immunogenic fragment of a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1-56. The method comprises a) combining the polypeptide with at least one test compound under conditions permissive for the activity of the polypeptide, b) assessing the activity of the polypeptide in the presence of the test compound, and c) comparing the activity of the polypeptide in the presence of the test compound with the activity of the  
30 polypeptide in the absence of the test compound, wherein a change in the activity of the polypeptide in the presence of the test compound is indicative of a compound that modulates the activity of the polypeptide.

Still yet another embodiment provides a method for screening a compound for effectiveness in altering expression of a target polynucleotide, wherein said target polynucleotide comprises a  
35 polynucleotide sequence selected from the group consisting of SEQ ID NO:57-112, the method

comprising a) exposing a sample comprising the target polynucleotide to a compound, b) detecting altered expression of the target polynucleotide, and c) comparing the expression of the target polynucleotide in the presence of varying amounts of the compound and in the absence of the compound.

- 5 Another embodiment provides a method for assessing toxicity of a test compound, said method comprising a) treating a biological sample containing nucleic acids with the test compound; b) hybridizing the nucleic acids of the treated biological sample with a probe comprising at least 20 contiguous nucleotides of a polynucleotide selected from the group consisting of i) a polynucleotide comprising a polynucleotide sequence selected from the group consisting of SEQ ID NO:57-112, ii) a
- 10 polynucleotide comprising a naturally occurring polynucleotide sequence at least 90% identical or at least about 90% identical to a polynucleotide sequence selected from the group consisting of SEQ ID NO:57-112, iii) a polynucleotide having a sequence complementary to i), iv) a polynucleotide complementary to the polynucleotide of ii), and v) an RNA equivalent of i)-iv). Hybridization occurs under conditions whereby a specific hybridization complex is formed between said probe and a target
- 15 polynucleotide in the biological sample, said target polynucleotide selected from the group consisting of i) a polynucleotide comprising a polynucleotide sequence selected from the group consisting of SEQ ID NO:57-112, ii) a polynucleotide comprising a naturally occurring polynucleotide sequence at least 90% identical or at least about 90% identical to a polynucleotide sequence selected from the group consisting of SEQ ID NO:57-112, iii) a polynucleotide complementary to the polynucleotide of
- 20 i), iv) a polynucleotide complementary to the polynucleotide of ii), and v) an RNA equivalent of i)-iv). Alternatively, the target polynucleotide can comprise a fragment of a polynucleotide selected from the group consisting of i)-v) above; c) quantifying the amount of hybridization complex; and d) comparing the amount of hybridization complex in the treated biological sample with the amount of hybridization complex in an untreated biological sample, wherein a difference in the amount of
- 25 hybridization complex in the treated biological sample is indicative of toxicity of the test compound.

### BRIEF DESCRIPTION OF THE TABLES

Table 1 summarizes the nomenclature for full length polynucleotide and polypeptide embodiments of the invention.

- 30 Table 2 shows the GenBank identification number and annotation of the nearest GenBank homolog for polypeptide embodiments of the invention. The probability scores for the matches between each polypeptide and its homolog(s) are also shown.

Table 3 shows structural features of polypeptide embodiments, including predicted motifs and domains, along with the methods, algorithms, and searchable databases used for analysis of the

35 polypeptides.

Table 4 lists the cDNA and/or genomic DNA fragments which were used to assemble polynucleotide embodiments, along with selected fragments of the polynucleotides.

Table 5 shows representative cDNA libraries for polynucleotide embodiments.

Table 6 provides an appendix which describes the tissues and vectors used for construction of the cDNA libraries shown in Table 5.

Table 7 shows the tools, programs, and algorithms used to analyze polynucleotides and polypeptides, along with applicable descriptions, references, and threshold parameters.

Table 8 shows single nucleotide polymorphisms found in polynucleotide embodiments, along with allele frequencies in different human populations.

## DESCRIPTION OF THE INVENTION

Before the present proteins, nucleic acids, and methods are described, it is understood that embodiments of the invention are not limited to the particular machines, instruments, materials, and methods described, as these may vary. It is also to be understood that the terminology used herein is for the purpose of describing particular embodiments only, and is not intended to limit the scope of the invention.

As used herein and in the appended claims, the singular forms "a," "an," and "the" include plural reference unless the context clearly dictates otherwise. Thus, for example, a reference to "a host cell" includes a plurality of such host cells, and a reference to "an antibody" is a reference to one or more antibodies and equivalents thereof known to those skilled in the art, and so forth.

Unless defined otherwise, all technical and scientific terms used herein have the same meanings as commonly understood by one of ordinary skill in the art to which this invention belongs. Although any machines, materials, and methods similar or equivalent to those described herein can be used to practice or test the present invention, the preferred machines, materials and methods are now described. All publications mentioned herein are cited for the purpose of describing and disclosing the cell lines, protocols, reagents and vectors which are reported in the publications and which might be used in connection with various embodiments of the invention. Nothing herein is to be construed as an admission that the invention is not entitled to antedate such disclosure by virtue of prior invention.

## DEFINITIONS

"MDDT" refers to the amino acid sequences of substantially purified MDDT obtained from any species, particularly a mammalian species, including bovine, ovine, porcine, murine, equine, and human, and from any source, whether natural, synthetic, semi-synthetic, or recombinant.

The term "agonist" refers to a molecule which intensifies or mimics the biological activity of MDDT. Agonists may include proteins, nucleic acids, carbohydrates, small molecules, or any other

compound or composition which modulates the activity of MDDT either by directly interacting with MDDT or by acting on components of the biological pathway in which MDDT participates.

An "allelic variant" is an alternative form of the gene encoding MDDT. Allelic variants may result from at least one mutation in the nucleic acid sequence and may result in altered mRNAs or in polypeptides whose structure or function may or may not be altered. A gene may have none, one, or many allelic variants of its naturally occurring form. Common mutational changes which give rise to allelic variants are generally ascribed to natural deletions, additions, or substitutions of nucleotides. Each of these types of changes may occur alone, or in combination with the others, one or more times in a given sequence.

10 "Altered" nucleic acid sequences encoding MDDT include those sequences with deletions, insertions, or substitutions of different nucleotides, resulting in a polypeptide the same as MDDT or a polypeptide with at least one functional characteristic of MDDT. Included within this definition are polymorphisms which may or may not be readily detectable using a particular oligonucleotide probe of the polynucleotide encoding MDDT, and improper or unexpected hybridization to allelic variants, 15 with a locus other than the normal chromosomal locus for the polynucleotide encoding MDDT. The encoded protein may also be "altered," and may contain deletions, insertions, or substitutions of amino acid residues which produce a silent change and result in a functionally equivalent MDDT. Deliberate amino acid substitutions may be made on the basis of one or more similarities in polarity, charge, solubility, hydrophobicity, hydrophilicity, and/or the amphipathic nature of the residues, as 20 long as the biological or immunological activity of MDDT is retained. For example, negatively charged amino acids may include aspartic acid and glutamic acid, and positively charged amino acids may include lysine and arginine. Amino acids with uncharged polar side chains having similar hydrophilicity values may include: asparagine and glutamine; and serine and threonine. Amino acids with uncharged side chains having similar hydrophilicity values may include: leucine, isoleucine, and 25 valine; glycine and alanine; and phenylalanine and tyrosine.

The terms "amino acid" and "amino acid sequence" can refer to an oligopeptide, a peptide, a polypeptide, or a protein sequence, or a fragment of any of these, and to naturally occurring or synthetic molecules. Where "amino acid sequence" is recited to refer to a sequence of a naturally occurring protein molecule, "amino acid sequence" and like terms are not meant to limit the amino acid sequence to the complete native amino acid sequence associated with the recited protein molecule. 30

"Amplification" relates to the production of additional copies of a nucleic acid. Amplification may be carried out using polymerase chain reaction (PCR) technologies or other nucleic acid amplification technologies well known in the art.

35 The term "antagonist" refers to a molecule which inhibits or attenuates the biological activity



of MDDT. Antagonists may include proteins such as antibodies, anticalins, nucleic acids, carbohydrates, small molecules, or any other compound or composition which modulates the activity of MDDT either by directly interacting with MDDT or by acting on components of the biological pathway in which MDDT participates.

5           The term "antibody" refers to intact immunoglobulin molecules as well as to fragments thereof, such as Fab, F(ab')<sub>2</sub>, and Fv fragments, which are capable of binding an epitopic determinant. Antibodies that bind MDDT polypeptides can be prepared using intact polypeptides or using fragments containing small peptides of interest as the immunizing antigen. The polypeptide or oligopeptide used to immunize an animal (e.g., a mouse, a rat, or a rabbit) can be derived from the  
10 translation of RNA, or synthesized chemically, and can be conjugated to a carrier protein if desired. Commonly used carriers that are chemically coupled to peptides include bovine serum albumin, thyroglobulin, and keyhole limpet hemocyanin (KLH). The coupled peptide is then used to immunize the animal.

          The term "antigenic determinant" refers to that region of a molecule (i.e., an epitope) that  
15 makes contact with a particular antibody. When a protein or a fragment of a protein is used to immunize a host animal, numerous regions of the protein may induce the production of antibodies which bind specifically to antigenic determinants (particular regions or three-dimensional structures on the protein). An antigenic determinant may compete with the intact antigen (i.e., the immunogen used to elicit the immune response) for binding to an antibody.

20           The term "aptamer" refers to a nucleic acid or oligonucleotide molecule that binds to a specific molecular target. Aptamers are derived from an *in vitro* evolutionary process (e.g., SELEX (Systematic Evolution of Ligands by EXponential Enrichment), described in U.S. Patent No. 5,270,163), which selects for target-specific aptamer sequences from large combinatorial libraries. Aptamer compositions may be double-stranded or single-stranded, and may include  
25 deoxyribonucleotides, ribonucleotides, nucleotide derivatives, or other nucleotide-like molecules. The nucleotide components of an aptamer may have modified sugar groups (e.g., the 2'-OH group of a ribonucleotide may be replaced by 2'-F or 2'-NH<sub>2</sub>), which may improve a desired property, e.g., resistance to nucleases or longer lifetime in blood. Aptamers may be conjugated to other molecules, e.g., a high molecular weight carrier to slow clearance of the aptamer from the circulatory system.  
30 Aptamers may be specifically cross-linked to their cognate ligands, e.g., by photo-activation of a cross-linker (Brody, E.N. and L. Gold (2000) J. Biotechnol. 74:5-13).

          The term "intramer" refers to an aptamer which is expressed *in vivo*. For example, a vaccinia virus-based RNA expression system has been used to express specific RNA aptamers at high levels in the cytoplasm of leukocytes (Blind, M. et al. (1999) Proc. Natl. Acad. Sci. USA 96:3606-3610).

35           The term "spiegelmer" refers to an aptamer which includes L-DNA, L-RNA, or other left-

handed nucleotide derivatives or nucleotide-like molecules. Aptamers containing left-handed nucleotides are resistant to degradation by naturally occurring enzymes, which normally act on substrates containing right-handed nucleotides.

The term "antisense" refers to any composition capable of base-pairing with the "sense" (coding) strand of a polynucleotide having a specific nucleic acid sequence. Antisense compositions may include DNA; RNA; peptide nucleic acid (PNA); oligonucleotides having modified backbone linkages such as phosphorothioates, methylphosphonates, or benzylphosphonates; oligonucleotides having modified sugar groups such as 2'-methoxyethyl sugars or 2'-methoxyethoxy sugars; or oligonucleotides having modified bases such as 5-methyl cytosine, 2'-deoxyuracil, or 7-deaza-2'-deoxyguanosine. Antisense molecules may be produced by any method including chemical synthesis or transcription. Once introduced into a cell, the complementary antisense molecule base-pairs with a naturally occurring nucleic acid sequence produced by the cell to form duplexes which block either transcription or translation. The designation "negative" or "minus" can refer to the antisense strand, and the designation "positive" or "plus" can refer to the sense strand of a reference DNA molecule.

The term "biologically active" refers to a protein having structural, regulatory, or biochemical functions of a naturally occurring molecule. Likewise, "immunologically active" or "immunogenic" refers to the capability of the natural, recombinant, or synthetic MDDT, or of any oligopeptide thereof, to induce a specific immune response in appropriate animals or cells and to bind with specific antibodies.

"Complementary" describes the relationship between two single-stranded nucleic acid sequences that anneal by base-pairing. For example, 5'-AGT-3' pairs with its complement, 3'-TCA-5'.

A "composition comprising a given polynucleotide" and a "composition comprising a given polypeptide" can refer to any composition containing the given polynucleotide or polypeptide. The composition may comprise a dry formulation or an aqueous solution. Compositions comprising polynucleotides encoding MDDT or fragments of MDDT may be employed as hybridization probes. The probes may be stored in freeze-dried form and may be associated with a stabilizing agent such as a carbohydrate. In hybridizations, the probe may be deployed in an aqueous solution containing salts (e.g., NaCl), detergents (e.g., sodium dodecyl sulfate; SDS), and other components (e.g., Denhardt's solution, dry milk, salmon sperm DNA, etc.).

"Consensus sequence" refers to a nucleic acid sequence which has been subjected to repeated DNA sequence analysis to resolve uncalled bases, extended using the XL-PCR kit (Applied Biosystems, Foster City CA) in the 5' and/or the 3' direction, and resequenced, or which has been assembled from one or more overlapping cDNA, EST, or genomic DNA fragments using a computer program for fragment assembly, such as the GELVIEW fragment assembly system (GCG, Madison

WI) or Phrap (University of Washington, Seattle WA). Some sequences have been both extended and assembled to produce the consensus sequence.

“Conservative amino acid substitutions” are those substitutions that are predicted to least interfere with the properties of the original protein, i.e., the structure and especially the function of the protein is conserved and not significantly changed by such substitutions. The table below shows amino acids which may be substituted for an original amino acid in a protein and which are regarded as conservative amino acid substitutions.

	Original Residue	Conservative Substitution
10	Ala	Gly, Ser
	Arg	His, Lys
	Asn	Asp, Gln, His
	Asp	Asn, Glu
	Cys	Ala, Ser
	Gln	Asn, Glu, His
15	Glu	Asp, Gln, His
	Gly	Ala
	His	Asn, Arg, Gln, Glu
	Ile	Leu, Val
	Leu	Ile, Val
20	Lys	Arg, Gln, Glu
	Met	Leu, Ile
	Phe	His, Met, Leu, Trp, Tyr
	Ser	Cys, Thr
	Thr	Ser, Val
25	Trp	Phe, Tyr
	Tyr	His, Phe, Trp
	Val	Ile, Leu, Thr

Conservative amino acid substitutions generally maintain (a) the structure of the polypeptide backbone in the area of the substitution, for example, as a beta sheet or alpha helical conformation, (b) the charge or hydrophobicity of the molecule at the site of the substitution, and/or (c) the bulk of the side chain.

A “deletion” refers to a change in the amino acid or nucleotide sequence that results in the absence of one or more amino acid residues or nucleotides.

The term “derivative” refers to a chemically modified polynucleotide or polypeptide. Chemical modifications of a polynucleotide can include, for example, replacement of hydrogen by an alkyl, acyl, hydroxyl, or amino group. A derivative polynucleotide encodes a polypeptide which retains at least one biological or immunological function of the natural molecule. A derivative polypeptide is one modified by glycosylation, pegylation, or any similar process that retains at least one biological or immunological function of the polypeptide from which it was derived.

A “detectable label” refers to a reporter molecule or enzyme that is capable of generating a measurable signal and is covalently or noncovalently joined to a polynucleotide or polypeptide.

“Differential expression” refers to increased or upregulated; or decreased, downregulated, or absent gene or protein expression, determined by comparing at least two different samples. Such comparisons may be carried out between, for example, a treated and an untreated sample, or a diseased and a normal sample.

5 “Exon shuffling” refers to the recombination of different coding regions (exons). Since an exon may represent a structural or functional domain of the encoded protein, new proteins may be assembled through the novel reassortment of stable substructures, thus allowing acceleration of the evolution of new protein functions.

A “fragment” is a unique portion of MDDT or a polynucleotide encoding MDDT which can  
10 be identical in sequence to, but shorter in length than, the parent sequence. A fragment may comprise up to the entire length of the defined sequence, minus one nucleotide/amino acid residue. For example, a fragment may comprise from about 5 to about 1000 contiguous nucleotides or amino acid residues. A fragment used as a probe, primer, antigen, therapeutic molecule, or for other purposes, may be at least 5, 10, 15, 16, 20, 25, 30, 40, 50, 60, 75, 100, 150, 250 or at least 500 contiguous  
15 nucleotides or amino acid residues in length. Fragments may be preferentially selected from certain regions of a molecule. For example, a polypeptide fragment may comprise a certain length of contiguous amino acids selected from the first 250 or 500 amino acids (or first 25% or 50%) of a polypeptide as shown in a certain defined sequence. Clearly these lengths are exemplary, and any length that is supported by the specification, including the Sequence Listing, tables, and figures, may  
20 be encompassed by the present embodiments.

A fragment of SEQ ID NO:57-112 can comprise a region of unique polynucleotide sequence that specifically identifies SEQ ID NO:57-112, for example, as distinct from any other sequence in the genome from which the fragment was obtained. A fragment of SEQ ID NO:57-112 can be employed in one or more embodiments of methods of the invention, for example, in hybridization and  
25 amplification technologies and in analogous methods that distinguish SEQ ID NO:57-112 from related polynucleotides. The precise length of a fragment of SEQ ID NO:57-112 and the region of SEQ ID NO:57-112 to which the fragment corresponds are routinely determinable by one of ordinary skill in the art based on the intended purpose for the fragment.

A fragment of SEQ ID NO:1-56 is encoded by a fragment of SEQ ID NO:57-112. A  
30 fragment of SEQ ID NO:1-56 can comprise a region of unique amino acid sequence that specifically identifies SEQ ID NO:1-56. For example, a fragment of SEQ ID NO:1-56 can be used as an immunogenic peptide for the development of antibodies that specifically recognize SEQ ID NO:1-56. The precise length of a fragment of SEQ ID NO:1-56 and the region of SEQ ID NO:1-56 to which the fragment corresponds can be determined based on the intended purpose for the fragment using one or  
35 more analytical methods described herein or otherwise known in the art.

A "full length" polynucleotide is one containing at least a translation initiation codon (e.g., methionine) followed by an open reading frame and a translation termination codon. A "full length" polynucleotide sequence encodes a "full length" polypeptide sequence.

"Homology" refers to sequence similarity or, interchangeably, sequence identity, between  
5 two or more polynucleotide sequences or two or more polypeptide sequences.

The terms "percent identity" and "% identity," as applied to polynucleotide sequences, refer to the percentage of residue matches between at least two polynucleotide sequences aligned using a standardized algorithm. Such an algorithm may insert, in a standardized and reproducible way, gaps in the sequences being compared in order to optimize alignment between two sequences, and  
10 therefore achieve a more meaningful comparison of the two sequences.

Percent identity between polynucleotide sequences may be determined using one or more computer algorithms or programs known in the art or described herein. For example, percent identity can be determined using the default parameters of the CLUSTAL V algorithm as incorporated into the MEGALIGN version 3.12e sequence alignment program. This program is part of the  
15 LASERGENE software package, a suite of molecular biological analysis programs (DNASTAR, Madison WI). CLUSTAL V is described in Higgins, D.G. and P.M. Sharp (1989; CABIOS 5:151-153) and in Higgins, D.G. et al. (1992; CABIOS 8:189-191). For pairwise alignments of polynucleotide sequences, the default parameters are set as follows: Ktuple=2, gap penalty=5, window=4, and "diagonals saved"=4. The "weighted" residue weight table is selected as the default.  
20 Percent identity is reported by CLUSTAL V as the "percent similarity" between aligned polynucleotide sequences.

Alternatively, a suite of commonly used and freely available sequence comparison algorithms which can be used is provided by the National Center for Biotechnology Information (NCBI) Basic Local Alignment Search Tool (BLAST) (Altschul, S.F. et al. (1990) J. Mol. Biol. 215:403-410),  
25 which is available from several sources, including the NCBI, Bethesda, MD, and on the Internet at <http://www.ncbi.nlm.nih.gov/BLAST/>. The BLAST software suite includes various sequence analysis programs including "blastn," that is used to align a known polynucleotide sequence with other polynucleotide sequences from a variety of databases. Also available is a tool called "BLAST 2 Sequences" that is used for direct pairwise comparison of two nucleotide sequences. "BLAST 2  
30 Sequences" can be accessed and used interactively at <http://www.ncbi.nlm.nih.gov/gorf/bl2.html>. The "BLAST 2 Sequences" tool can be used for both blastn and blastp (discussed below). BLAST programs are commonly used with gap and other parameters set to default settings. For example, to compare two nucleotide sequences, one may use blastn with the "BLAST 2 Sequences" tool Version 2.0.12 (April-21-2000) set at default parameters. Such default parameters may be, for example:

35 *Matrix: BLOSUM62*

*Reward for match: 1*

*Penalty for mismatch: -2*

*Open Gap: 5 and Extension Gap: 2 penalties*

*Gap x drop-off: 50*

5 *Expect: 10*

*Word Size: 11*

*Filter: on*

Percent identity may be measured over the length of an entire defined sequence, for example, as defined by a particular SEQ ID number, or may be measured over a shorter length, for example, over the length of a fragment taken from a larger, defined sequence, for instance, a fragment of at least 20, at least 30, at least 40, at least 50, at least 70, at least 100, or at least 200 contiguous nucleotides. Such lengths are exemplary only, and it is understood that any fragment length supported by the sequences shown herein, in the tables, figures, or Sequence Listing, may be used to describe a length over which percentage identity may be measured.

15 Nucleic acid sequences that do not show a high degree of identity may nevertheless encode similar amino acid sequences due to the degeneracy of the genetic code. It is understood that changes in a nucleic acid sequence can be made using this degeneracy to produce multiple nucleic acid sequences that all encode substantially the same protein.

The phrases "percent identity" and "% identity," as applied to polypeptide sequences, refer to the percentage of residue matches between at least two polypeptide sequences aligned using a standardized algorithm. Methods of polypeptide sequence alignment are well-known. Some alignment methods take into account conservative amino acid substitutions. Such conservative substitutions, explained in more detail above, generally preserve the charge and hydrophobicity at the site of substitution, thus preserving the structure (and therefore function) of the polypeptide.

25 Percent identity between polypeptide sequences may be determined using the default parameters of the CLUSTAL V algorithm as incorporated into the MEGALIGN version 3.12e sequence alignment program (described and referenced above). For pairwise alignments of polypeptide sequences using CLUSTAL V, the default parameters are set as follows: Ktuple=1, gap penalty=3, window=5, and "diagonals saved"=5. The PAM250 matrix is selected as the default residue weight table. As with polynucleotide alignments, the percent identity is reported by CLUSTAL V as the "percent similarity" between aligned polypeptide sequence pairs.

Alternatively the NCBI BLAST software suite may be used. For example, for a pairwise comparison of two polypeptide sequences, one may use the "BLAST 2 Sequences" tool Version 2.0.12 (April-21-2000) with blastp set at default parameters. Such default parameters may be, for example:

*Matrix: BLOSUM62*

*Open Gap: 11 and Extension Gap: 1 penalties*

*Gap x drop-off: 50*

*Expect: 10*

5 *Word Size: 3*

*Filter: on*

Percent identity may be measured over the length of an entire defined polypeptide sequence, for example, as defined by a particular SEQ ID number, or may be measured over a shorter length, for example, over the length of a fragment taken from a larger, defined polypeptide sequence, for instance, a fragment of at least 15, at least 20, at least 30, at least 40, at least 50, at least 70 or at least 150 contiguous residues. Such lengths are exemplary only, and it is understood that any fragment length supported by the sequences shown herein, in the tables, figures or Sequence Listing, may be used to describe a length over which percentage identity may be measured.

15 "Human artificial chromosomes" (HACs) are linear microchromosomes which may contain DNA sequences of about 6 kb to 10 Mb in size and which contain all of the elements required for chromosome replication, segregation and maintenance.

The term "humanized antibody" refers to an antibody molecule in which the amino acid sequence in the non-antigen binding regions has been altered so that the antibody more closely resembles a human antibody, and still retains its original binding ability.

20 "Hybridization" refers to the process by which a polynucleotide strand anneals with a complementary strand through base pairing under defined hybridization conditions. Specific hybridization is an indication that two nucleic acid sequences share a high degree of complementarity. Specific hybridization complexes form under permissive annealing conditions and remain hybridized after the "washing" step(s). The washing step(s) is particularly important in determining the stringency of the hybridization process, with more stringent conditions allowing less non-specific binding, i.e., binding between pairs of nucleic acid strands that are not perfectly matched. Permissive conditions for annealing of nucleic acid sequences are routinely determinable by one of ordinary skill in the art and may be consistent among hybridization experiments, whereas wash conditions may be varied among experiments to achieve the desired stringency, and therefore hybridization specificity.

30 Permissive annealing conditions occur, for example, at 68°C in the presence of about 6 x SSC, about 1% (w/v) SDS, and about 100 µg/ml sheared, denatured salmon sperm DNA.

Generally, stringency of hybridization is expressed, in part, with reference to the temperature under which the wash step is carried out. Such wash temperatures are typically selected to be about 5°C to 20°C lower than the thermal melting point ( $T_m$ ) for the specific sequence at a defined ionic strength and pH. The  $T_m$  is the temperature (under defined ionic strength and pH) at which 50% of

the target sequence hybridizes to a perfectly matched probe. An equation for calculating  $T_m$  and conditions for nucleic acid hybridization are well known and can be found in Sambrook, J. et al. (1989) Molecular Cloning: A Laboratory Manual, 2<sup>nd</sup> ed., vol. 1-3, Cold Spring Harbor Press, Plainview NY; specifically see volume 2, chapter 9.

5 High stringency conditions for hybridization between polynucleotides of the present invention include wash conditions of 68°C in the presence of about 0.2 x SSC and about 0.1% SDS, for 1 hour. Alternatively, temperatures of about 65°C, 60°C, 55°C, or 42°C may be used. SSC concentration may be varied from about 0.1 to 2 x SSC, with SDS being present at about 0.1%. Typically, blocking reagents are used to block non-specific hybridization. Such blocking reagents  
10 include, for instance, sheared and denatured salmon sperm DNA at about 100-200 µg/ml. Organic solvent, such as formamide at a concentration of about 35-50% v/v, may also be used under particular circumstances, such as for RNA:DNA hybridizations. Useful variations on these wash conditions will be readily apparent to those of ordinary skill in the art. Hybridization, particularly under high stringency conditions, may be suggestive of evolutionary similarity between the nucleotides. Such  
15 similarity is strongly indicative of a similar role for the nucleotides and their encoded polypeptides.

The term "hybridization complex" refers to a complex formed between two nucleic acids by virtue of the formation of hydrogen bonds between complementary bases. A hybridization complex may be formed in solution (e.g.,  $C_0t$  or  $R_0t$  analysis) or formed between one nucleic acid present in solution and another nucleic acid immobilized on a solid support (e.g., paper, membranes, filters,  
20 chips, pins or glass slides, or any other appropriate substrate to which cells or their nucleic acids have been fixed).

The words "insertion" and "addition" refer to changes in an amino acid or polynucleotide sequence resulting in the addition of one or more amino acid residues or nucleotides, respectively.

"Immune response" can refer to conditions associated with inflammation, trauma, immune  
25 disorders, or infectious or genetic disease, etc. These conditions can be characterized by expression of various factors, e.g., cytokines, chemokines, and other signaling molecules, which may affect cellular and systemic defense systems.

An "immunogenic fragment" is a polypeptide or oligopeptide fragment of MDDT which is capable of eliciting an immune response when introduced into a living organism, for example, a  
30 mammal. The term "immunogenic fragment" also includes any polypeptide or oligopeptide fragment of MDDT which is useful in any of the antibody production methods disclosed herein or known in the art.

The term "microarray" refers to an arrangement of a plurality of polynucleotides, polypeptides, antibodies, or other chemical compounds on a substrate.

35 The terms "element" and "array element" refer to a polynucleotide, polypeptide, antibody, or



other chemical compound having a unique and defined position on a microarray.

The term "modulate" refers to a change in the activity of MDDT. For example, modulation may cause an increase or a decrease in protein activity, binding characteristics, or any other biological, functional, or immunological properties of MDDT.

5       The phrases "nucleic acid" and "nucleic acid sequence" refer to a nucleotide, oligonucleotide, polynucleotide, or any fragment thereof. These phrases also refer to DNA or RNA of genomic or synthetic origin which may be single-stranded or double-stranded and may represent the sense or the antisense strand, to peptide nucleic acid (PNA), or to any DNA-like or RNA-like material.

10       "Operably linked" refers to the situation in which a first nucleic acid sequence is placed in a functional relationship with a second nucleic acid sequence. For instance, a promoter is operably linked to a coding sequence if the promoter affects the transcription or expression of the coding sequence. Operably linked DNA sequences may be in close proximity or contiguous and, where necessary to join two protein coding regions, in the same reading frame.

15       "Peptide nucleic acid" (PNA) refers to an antisense molecule or anti-gene agent which comprises an oligonucleotide of at least about 5 nucleotides in length linked to a peptide backbone of amino acid residues ending in lysine. The terminal lysine confers solubility to the composition. PNAs preferentially bind complementary single stranded DNA or RNA and stop transcript elongation, and may be pegylated to extend their lifespan in the cell.

20       "Post-translational modification" of an MDDT may involve lipidation, glycosylation, phosphorylation, acetylation, racemization, proteolytic cleavage, and other modifications known in the art. These processes may occur synthetically or biochemically. Biochemical modifications will vary by cell type depending on the enzymatic milieu of MDDT.

25       "Probe" refers to nucleic acids encoding MDDT, their complements, or fragments thereof, which are used to detect identical, allelic or related nucleic acids. Probes are isolated oligonucleotides or polynucleotides attached to a detectable label or reporter molecule. Typical labels include radioactive isotopes, ligands, chemiluminescent agents, and enzymes. "Primers" are short nucleic acids, usually DNA oligonucleotides, which may be annealed to a target polynucleotide by complementary base-pairing. The primer may then be extended along the target DNA strand by a DNA polymerase enzyme. Primer pairs can be used for amplification (and identification) of a nucleic acid, e.g., by the polymerase chain reaction (PCR).

30       Probes and primers as used in the present invention typically comprise at least 15 contiguous nucleotides of a known sequence. In order to enhance specificity, longer probes and primers may also be employed, such as probes and primers that comprise at least 20, 25, 30, 40, 50, 60, 70, 80, 90, 100, or at least 150 consecutive nucleotides of the disclosed nucleic acid sequences. Probes and primers  
35       may be considerably longer than these examples, and it is understood that any length supported by the

specification, including the tables, figures, and Sequence Listing, may be used.

Methods for preparing and using probes and primers are described in the references, for example Sambrook, J. et al. (1989; Molecular Cloning: A Laboratory Manual, 2<sup>nd</sup> ed., vol. 1-3, Cold Spring Harbor Press, Plainview NY), Ausubel, F.M. et al. (1999) Short Protocols in Molecular  
5 Biology, 4<sup>th</sup> ed., John Wiley & Sons, New York NY), and Innis, M. et al. (1990; PCR Protocols, A Guide to Methods and Applications, Academic Press, San Diego CA). PCR primer pairs can be derived from a known sequence, for example, by using computer programs intended for that purpose such as Primer (Version 0.5, 1991, Whitehead Institute for Biomedical Research, Cambridge MA).

Oligonucleotides for use as primers are selected using software known in the art for such  
10 purpose. For example, OLIGO 4.06 software is useful for the selection of PCR primer pairs of up to 100 nucleotides each, and for the analysis of oligonucleotides and larger polynucleotides of up to 5,000 nucleotides from an input polynucleotide sequence of up to 32 kilobases. Similar primer selection programs have incorporated additional features for expanded capabilities. For example, the PrimOU primer selection program (available to the public from the Genome Center at University of  
15 Texas South West Medical Center, Dallas TX) is capable of choosing specific primers from megabase sequences and is thus useful for designing primers on a genome-wide scope. The Primer3 primer selection program (available to the public from the Whitehead Institute/MIT Center for Genome Research, Cambridge MA) allows the user to input a "mispriming library," in which sequences to avoid as primer binding sites are user-specified. Primer3 is useful, in particular, for the  
20 selection of oligonucleotides for microarrays. (The source code for the latter two primer selection programs may also be obtained from their respective sources and modified to meet the user's specific needs.) The PrimeGen program (available to the public from the UK Human Genome Mapping Project Resource Centre, Cambridge UK) designs primers based on multiple sequence alignments, thereby allowing selection of primers that hybridize to either the most conserved or least conserved  
25 regions of aligned nucleic acid sequences. Hence, this program is useful for identification of both unique and conserved oligonucleotides and polynucleotide fragments. The oligonucleotides and polynucleotide fragments identified by any of the above selection methods are useful in hybridization technologies, for example, as PCR or sequencing primers, microarray elements, or specific probes to identify fully or partially complementary polynucleotides in a sample of nucleic acids. Methods of  
30 oligonucleotide selection are not limited to those described above.

A "recombinant nucleic acid" is a nucleic acid that is not naturally occurring or has a sequence that is made by an artificial combination of two or more otherwise separated segments of sequence. This artificial combination is often accomplished by chemical synthesis or, more commonly, by the artificial manipulation of isolated segments of nucleic acids, e.g., by genetic  
35 engineering techniques such as those described in Sambrook, *supra*. The term recombinant includes

nucleic acids that have been altered solely by addition, substitution, or deletion of a portion of the nucleic acid. Frequently, a recombinant nucleic acid may include a nucleic acid sequence operably linked to a promoter sequence. Such a recombinant nucleic acid may be part of a vector that is used, for example, to transform a cell.

5           Alternatively, such recombinant nucleic acids may be part of a viral vector, e.g., based on a vaccinia virus, that could be used to vaccinate a mammal wherein the recombinant nucleic acid is expressed, inducing a protective immunological response in the mammal.

          A "regulatory element" refers to a nucleic acid sequence usually derived from untranslated regions of a gene and includes enhancers, promoters, introns, and 5' and 3' untranslated regions  
10 (UTRs). Regulatory elements interact with host or viral proteins which control transcription, translation, or RNA stability.

          "Reporter molecules" are chemical or biochemical moieties used for labeling a nucleic acid, amino acid, or antibody. Reporter molecules include radionuclides; enzymes; fluorescent, chemiluminescent, or chromogenic agents; substrates; cofactors; inhibitors; magnetic particles; and  
15 other moieties known in the art.

          An "RNA equivalent," in reference to a DNA molecule, is composed of the same linear sequence of nucleotides as the reference DNA molecule with the exception that all occurrences of the nitrogenous base thymine are replaced with uracil, and the sugar backbone is composed of ribose instead of deoxyribose.

20           The term "sample" is used in its broadest sense. A sample suspected of containing MDDT, nucleic acids encoding MDDT, or fragments thereof may comprise a bodily fluid; an extract from a cell, chromosome, organelle, or membrane isolated from a cell; a cell; genomic DNA, RNA, or cDNA, in solution or bound to a substrate; a tissue; a tissue print; etc.

          The terms "specific binding" and "specifically binding" refer to that interaction between a  
25 protein or peptide and an agonist, an antibody, an antagonist, a small molecule, or any natural or synthetic binding composition. The interaction is dependent upon the presence of a particular structure of the protein, e.g., the antigenic determinant or epitope, recognized by the binding molecule. For example, if an antibody is specific for epitope "A," the presence of a polypeptide comprising the epitope A, or the presence of free unlabeled A, in a reaction containing free labeled A  
30 and the antibody will reduce the amount of labeled A that binds to the antibody.

          The term "substantially purified" refers to nucleic acid or amino acid sequences that are removed from their natural environment and are isolated or separated, and are at least about 60% free, preferably at least about 75% free, and most preferably at least about 90% free from other components with which they are naturally associated.

35           A "substitution" refers to the replacement of one or more amino acid residues or nucleotides

by different amino acid residues or nucleotides, respectively.

"Substrate" refers to any suitable rigid or semi-rigid support including membranes, filters, chips, slides, wafers, fibers, magnetic or nonmagnetic beads, gels, tubing, plates, polymers, microparticles and capillaries. The substrate can have a variety of surface forms, such as wells, trenches, pins, channels and pores, to which polynucleotides or polypeptides are bound.

A "transcript image" or "expression profile" refers to the collective pattern of gene expression by a particular cell type or tissue under given conditions at a given time.

"Transformation" describes a process by which exogenous DNA is introduced into a recipient cell. Transformation may occur under natural or artificial conditions according to various methods well known in the art, and may rely on any known method for the insertion of foreign nucleic acid sequences into a prokaryotic or eukaryotic host cell. The method for transformation is selected based on the type of host cell being transformed and may include, but is not limited to, bacteriophage or viral infection, electroporation, heat shock, lipofection, and particle bombardment. The term "transformed cells" includes stably transformed cells in which the inserted DNA is capable of replication either as an autonomously replicating plasmid or as part of the host chromosome, as well as transiently transformed cells which express the inserted DNA or RNA for limited periods of time.

A "transgenic organism," as used herein, is any organism, including but not limited to animals and plants, in which one or more of the cells of the organism contains heterologous nucleic acid introduced by way of human intervention, such as by transgenic techniques well known in the art. The nucleic acid is introduced into the cell, directly or indirectly by introduction into a precursor of the cell, by way of deliberate genetic manipulation, such as by microinjection or by infection with a recombinant virus. In another embodiment, the nucleic acid can be introduced by infection with a recombinant viral vector, such as a lentiviral vector (Lois, C. et al. (2002) Science 295:868-872). The term genetic manipulation does not include classical cross-breeding, or *in vitro* fertilization, but rather is directed to the introduction of a recombinant DNA molecule. The transgenic organisms contemplated in accordance with the present invention include bacteria, cyanobacteria, fungi, plants and animals. The isolated DNA of the present invention can be introduced into the host by methods known in the art, for example infection, transfection, transformation or transconjugation. Techniques for transferring the DNA of the present invention into such organisms are widely known and provided in references such as Sambrook et al. (1989), *supra*.

A "variant" of a particular nucleic acid sequence is defined as a nucleic acid sequence having at least 40% sequence identity to the particular nucleic acid sequence over a certain length of one of the nucleic acid sequences using blastn with the "BLAST 2 Sequences" tool Version 2.0.9 (May-07-1999) set at default parameters. Such a pair of nucleic acids may show, for example, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least

93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% or greater sequence identity over a certain defined length. A variant may be described as, for example, an "allelic" (as defined above), "splice," "species," or "polymorphic" variant. A splice variant may have significant identity to a reference molecule, but will generally have a greater or lesser number of polynucleotides due to alternate splicing of exons during mRNA processing. The corresponding polypeptide may possess additional functional domains or lack domains that are present in the reference molecule. Species variants are polynucleotides that vary from one species to another. The resulting polypeptides will generally have significant amino acid identity relative to each other. A polymorphic variant is a variation in the polynucleotide sequence of a particular gene between individuals of a given species. Polymorphic variants also may encompass "single nucleotide polymorphisms" (SNPs) in which the polynucleotide sequence varies by one nucleotide base. The presence of SNPs may be indicative of, for example, a certain population, a disease state, or a propensity for a disease state.

A "variant" of a particular polypeptide sequence is defined as a polypeptide sequence having at least 40% sequence identity to the particular polypeptide sequence over a certain length of one of the polypeptide sequences using blastp with the "BLAST 2 Sequences" tool Version 2.0.9 (May-07-1999) set at default parameters. Such a pair of polypeptides may show, for example, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% or greater sequence identity over a certain defined length of one of the polypeptides.

## THE INVENTION

Various embodiments of the invention include new human molecules for disease detection and treatment (MDDT), the polynucleotides encoding MDDT, and the use of these compositions for the diagnosis, treatment, or prevention of cell proliferative, autoimmune/inflammatory, developmental, and neurological disorders, diseases treated with steroids and disorders caused by the metabolic response to treatment with steroids.

Table 1 summarizes the nomenclature for the full length polynucleotide and polypeptide embodiments of the invention. Each polynucleotide and its corresponding polypeptide are correlated to a single Incyte project identification number (Incyte Project ID). Each polypeptide sequence is denoted by both a polypeptide sequence identification number (Polypeptide SEQ ID NO:) and an Incyte polypeptide sequence number (Incyte Polypeptide ID) as shown. Each polynucleotide sequence is denoted by both a polynucleotide sequence identification number (Polynucleotide SEQ ID NO:) and an Incyte polynucleotide consensus sequence number (Incyte Polynucleotide ID) as shown. Column 6 shows the Incyte ID numbers of physical, full length clones corresponding to

polypeptide and polynucleotide embodiments. The full length clones encode polypeptides which have at least 95% sequence identity to the polypeptides shown in column 3.

Table 2 shows sequences with homology to the polypeptides of the invention as identified by BLAST analysis against the GenBank protein (genpept) database. Columns 1 and 2 show the polypeptide sequence identification number (Polypeptide SEQ ID NO:) and the corresponding Incyte polypeptide sequence number (Incyte Polypeptide ID) for polypeptides of the invention. Column 3 shows the GenBank identification number (GenBank ID NO:) of the nearest GenBank homolog. Column 4 shows the probability scores for the matches between each polypeptide and its homolog(s). Column 5 shows the annotation of the GenBank homolog(s) along with relevant citations where applicable, all of which are expressly incorporated by reference herein.

Table 3 shows various structural features of the polypeptides of the invention. Columns 1 and 2 show the polypeptide sequence identification number (SEQ ID NO:) and the corresponding Incyte polypeptide sequence number (Incyte Polypeptide ID) for each polypeptide of the invention. Column 3 shows the number of amino acid residues in each polypeptide. Column 4 shows potential phosphorylation sites, and column 5 shows potential glycosylation sites, as determined by the MOTIFS program of the GCG sequence analysis software package (Genetics Computer Group, Madison WI). Column 6 shows amino acid residues comprising signature sequences, domains, and motifs. Column 7 shows analytical methods for protein structure/function analysis and in some cases, searchable databases to which the analytical methods were applied.

Together, Tables 2 and 3 summarize the properties of polypeptides of the invention, and these properties establish that the claimed polypeptides are molecules for disease detection and treatment. For example, SEQ ID NO:2 contains a potassium channel tetramerisation domain as determined by searching for statistically significant matches in the hidden Markov model (HMM)-based PFAM database of conserved protein family domains. (See Table 3.)

In another example, SEQ ID NO:22 is 93% identical, from residue M1 to residue V1451, to mouse pecanex 1, which is the mouse homolog of *Drosophila* pecanex, a maternal-effect neurogenic protein (GenBank ID g6650377) as determined by the Basic Local Alignment Search Tool (BLAST). (See Table 2.) The BLAST probability score is 0.0, which indicates the probability of obtaining the observed polypeptide sequence alignment by chance. Data from further BLAST analyses provide corroborative evidence that SEQ ID NO:22 is a pecanex 1 protein.

In another example, SEQ ID NO:31 is 33% identical, from residue R17 to residue G452, to *Drosophila melanogaster* Diablo (GenBank ID g7243777) as determined by the Basic Local Alignment Search- Tool (BLAST). (See Table 2.) The BLAST probability score is 2.9e-50, which indicates the probability of obtaining the observed polypeptide sequence alignment by chance. SEQ ID NO:31 also contains a BTB-POZ protein interaction domain as determined by searching for

statistically significant matches in the hidden Markov model (HMM)-based PFAM database of conserved protein family domains. (See Table 3.) Data from BLIMPS and additional BLAST analyses provide further corroborative evidence that SEQ ID NO:31 is an apoptosis-associated protein.

5 In another example, SEQ ID NO:36 is 62% identical, from residue E84 to residue L370, to a human EVI-5 protein (GenBank ID g3093476) as determined by the Basic Local Alignment Search Tool (BLAST). (See Table 2.) The BLAST probability score is 6.9e-90, which indicates the probability of obtaining the observed polypeptide sequence alignment by chance. Data from MOTIFS analysis provides further corroborative evidence that SEQ ID NO:36 is a protein with  
10 potential utility for disease detection or treatment.

In another example, SEQ ID NO:44 is 78% identical, from residue D224 to residue V838, and 98% identical, from residue M1 to residue W333, to human sporulation-induced transcript 4 (SIT4)-associated protein SAPLa (GenBank ID g11527201) as determined by the Basic Local Alignment Search Tool (BLAST). (See Table 2.) The BLAST probability score is 6.7e-250 for the  
15 first homologous section and 1.8e-171 for the second, which indicates the probability of obtaining the observed polypeptide sequence alignment by chance. Data from other BLAST analyses provide further corroborative evidence that SEQ ID NO:44 is a cycle cell phosphorylation sit4-associating protein (a protein which associates with the sit4 phosphatase in a cell cycle-dependent manner).

In another example, SEQ ID NO:47 is 52% identical, from residue F6 to residue L256, to a  
20 WD-40-containing *Xenopus laevis* protein that is upregulated by thyroid hormone (GenBank ID g1314316) as determined by the Basic Local Alignment Search Tool (BLAST). The BLAST probability score is 6.3e-73, which indicates the probability of obtaining the observed polypeptide sequence alignment by chance. SEQ ID NO:47 also contains a WD, G-beta repeat domain as determined by searching for statistically significant matches in the hidden Markov model (HMM)-  
25 based PFAM database of conserved protein family domains. (See Table 3.) Data from MOTIFS and PROFILESCAN analyses provide further corroborative evidence that SEQ ID NO:47 is a full-length human molecule for disease detection and treatment. SEQ ID NO:1, SEQ ID NO:3-21, SEQ ID NO:23-30, SEQ ID NO:32-35, SEQ ID NO:37-43, SEQ ID NO:45-46 and SEQ ID NO:48-56 were analyzed and annotated in a similar manner. The algorithms and parameters for the analysis of SEQ  
30 ID NO:1-56 are described in Table 7.

As shown in Table 4, the full length polynucleotide embodiments were assembled using cDNA sequences or coding (exon) sequences derived from genomic DNA, or any combination of these two types of sequences. Column 1 lists the polynucleotide sequence identification number (Polynucleotide SEQ ID NO:), the corresponding Incyte polynucleotide consensus sequence number  
35 (Incyte ID) for each polynucleotide of the invention, and the length of each polynucleotide sequence

in basepairs. Column 2 shows the nucleotide start (5') and stop (3') positions of the cDNA and/or genomic sequences used to assemble the full length polynucleotide embodiments, and of fragments of the polynucleotides which are useful, for example, in hybridization or amplification technologies that identify SEQ ID NO:57-112 or that distinguish between SEQ ID NO:57-112 and related

5 polynucleotides.

The polynucleotide fragments described in Column 2 of Table 4 may refer specifically, for example, to Incyte cDNAs derived from tissue-specific cDNA libraries or from pooled cDNA libraries. Alternatively, the polynucleotide fragments described in column 2 may refer to GenBank cDNAs or ESTs which contributed to the assembly of the full length polynucleotides. In addition, the

10 polynucleotide fragments described in column 2 may identify sequences derived from the ENSEMBL (The Sanger Centre, Cambridge, UK) database (*i.e.*, those sequences including the designation "ENST"). Alternatively, the polynucleotide fragments described in column 2 may be derived from the NCBI RefSeq Nucleotide Sequence Records Database (*i.e.*, those sequences including the designation "NM" or "NT") or the NCBI RefSeq Protein Sequence Records (*i.e.*, those sequences

15 including the designation "NP"). Alternatively, the polynucleotide fragments described in column 2 may refer to assemblages of both cDNA and Genscan-predicted exons brought together by an "exon stitching" algorithm. For example, a polynucleotide sequence identified as

FL\_XXXXXX\_N<sub>1</sub>\_N<sub>2</sub>\_YYYYY\_N<sub>3</sub>\_N<sub>4</sub> represents a "stitched" sequence in which XXXXXX is the identification number of the cluster of sequences to which the algorithm was applied, and YYYYY is

20 the number of the prediction generated by the algorithm, and N<sub>1,2,3...</sub>, if present, represent specific exons that may have been manually edited during analysis (See Example V). Alternatively, the polynucleotide fragments in column 2 may refer to assemblages of exons brought together by an "exon-stretching" algorithm. For example, a polynucleotide sequence identified as

FLXXXXXX\_gAAAAA\_gBBBBB\_1\_N is a "stretched" sequence, with XXXXXX being the Incyte

25 project identification number, gAAAAA being the GenBank identification number of the human genomic sequence to which the "exon-stretching" algorithm was applied, gBBBBB being the GenBank identification number or NCBI RefSeq identification number of the nearest GenBank protein homolog, and N referring to specific exons (See Example V). In instances where a RefSeq sequence was used as a protein homolog for the "exon-stretching" algorithm, a RefSeq identifier

30 (denoted by "NM," "NP," or "NT") may be used in place of the GenBank identifier (*i.e.*, gBBBBB).

Alternatively, a prefix identifies component sequences that were hand-edited, predicted from genomic DNA sequences, or derived from a combination of sequence analysis methods. The following Table lists examples of component sequence prefixes and corresponding sequence analysis methods associated with the prefixes (see Example IV and Example V).



Prefix	Type of analysis and/or examples of programs
GNN, GFG, ENST	Exon prediction from genomic sequences using, for example, GENSCAN (Stanford University, CA, USA) or FGENES (Computer Genomics Group, The Sanger Centre, Cambridge, UK).
GBI	Hand-edited analysis of genomic sequences.
FL	Stitched or stretched genomic sequences (see Example V).
INCY	Full length transcript and exon prediction from mapping of EST sequences to the genome. Genomic location and EST composition data are combined to predict the exons and resulting transcript.

In some cases, Incyte cDNA coverage redundant with the sequence coverage shown in Table 4 was obtained to confirm the final consensus polynucleotide sequence, but the relevant Incyte cDNA identification numbers are not shown.

Table 5 shows the representative cDNA libraries for those full length polynucleotides which were assembled using Incyte cDNA sequences. The representative cDNA library is the Incyte cDNA library which is most frequently represented by the Incyte cDNA sequences which were used to assemble and confirm the above polynucleotides. The tissues and vectors which were used to construct the cDNA libraries shown in Table 5 are described in Table 6.

Table 8 shows single nucleotide polymorphisms (SNPs) found in polynucleotide embodiments, along with allele frequencies in different human populations. Columns 1 and 2 show the polynucleotide sequence identification number (SEQ ID NO:) and the corresponding Incyte project identification number (PID) for polynucleotides of the invention. Column 3 shows the Incyte identification number for the EST in which the SNP was detected (EST ID), and column 4 shows the identification number for the SNP (SNP ID). Column 5 shows the position within the EST sequence at which the SNP is located (EST SNP), and column 6 shows the position of the SNP within the full-length polynucleotide sequence (CB1 SNP). Column 7 shows the allele found in the EST sequence. Columns 8 and 9 show the two alleles found at the SNP site. Column 10 shows the amino acid encoded by the codon including the SNP site, based upon the allele found in the EST. Columns 11-14 show the frequency of allele 1 in four different human populations. An entry of n/d (not detected) indicates that the frequency of allele 1 in the population was too low to be detected, while n/a (not available) indicates that the allele frequency was not determined for the population.

The invention also encompasses MDDT variants. A preferred MDDT variant is one which has at least about 80%, or alternatively at least about 90%, or even at least about 95% amino acid sequence identity to the MDDT amino acid sequence, and which contains at least one functional or

structural characteristic of MDDT.

Various embodiments also encompass polynucleotides which encode MDDT. In a particular embodiment, the invention encompasses a polynucleotide sequence comprising a sequence selected from the group consisting of SEQ ID NO:57-112, which encodes MDDT. The polynucleotide  
5 sequences of SEQ ID NO:57-112, as presented in the Sequence Listing, embrace the equivalent RNA sequences, wherein occurrences of the nitrogenous base thymine are replaced with uracil, and the sugar backbone is composed of ribose instead of deoxyribose.

The invention also encompasses variants of a polynucleotide encoding MDDT. In particular, such a variant polynucleotide will have at least about 70%, or alternatively at least about 85%, or  
10 even at least about 95% polynucleotide sequence identity to a polynucleotide encoding MDDT. A particular aspect of the invention encompasses a variant of a polynucleotide comprising a sequence selected from the group consisting of SEQ ID NO:57-112 which has at least about 70%, or alternatively at least about 85%, or even at least about 95% polynucleotide sequence identity to a nucleic acid sequence selected from the group consisting of SEQ ID NO:57-112. Any one of the  
15 polynucleotide variants described above can encode a polypeptide which contains at least one functional or structural characteristic of MDDT.

In addition, or in the alternative, a polynucleotide variant of the invention is a splice variant of a polynucleotide encoding MDDT. A splice variant may have portions which have significant sequence identity to a polynucleotide encoding MDDT, but will generally have a greater or lesser  
20 number of polynucleotides due to additions or deletions of blocks of sequence arising from alternate splicing of exons during mRNA processing. A splice variant may have less than about 70%, or alternatively less than about 60%, or alternatively less than about 50% polynucleotide sequence identity to a polynucleotide encoding MDDT over its entire length; however, portions of the splice variant will have at least about 70%, or alternatively at least about 85%, or alternatively at least about  
25 95%, or alternatively 100% polynucleotide sequence identity to portions of the polynucleotide encoding MDDT. For example, a polynucleotide comprising a sequence of SEQ ID NO:112 and a polynucleotide comprising a sequence of SEQ ID NO:59 are splice variants of each other. Any one of the splice variants described above can encode a polypeptide which contains at least one functional or structural characteristic of MDDT.

30 It will be appreciated by those skilled in the art that as a result of the degeneracy of the genetic code, a multitude of polynucleotide sequences encoding MDDT, some bearing minimal similarity to the polynucleotide sequences of any known and naturally occurring gene, may be produced. Thus, the invention contemplates each and every possible variation of polynucleotide sequence that could be made by selecting combinations based on possible codon choices. These  
35 combinations are made in accordance with the standard triplet genetic code as applied to the

polynucleotide sequence of naturally occurring MDDT, and all such variations are to be considered as being specifically disclosed.

Although polynucleotides which encode MDDT and its variants are generally capable of hybridizing to polynucleotides encoding naturally occurring MDDT under appropriately selected conditions of stringency, it may be advantageous to produce polynucleotides encoding MDDT or its derivatives possessing a substantially different codon usage, e.g., inclusion of non-naturally occurring codons. Codons may be selected to increase the rate at which expression of the peptide occurs in a particular prokaryotic or eukaryotic host in accordance with the frequency with which particular codons are utilized by the host. Other reasons for substantially altering the nucleotide sequence encoding MDDT and its derivatives without altering the encoded amino acid sequences include the production of RNA transcripts having more desirable properties, such as a greater half-life, than transcripts produced from the naturally occurring sequence.

The invention also encompasses production of polynucleotides which encode MDDT and MDDT derivatives, or fragments thereof, entirely by synthetic chemistry. After production, the synthetic polynucleotide may be inserted into any of the many available expression vectors and cell systems using reagents well known in the art. Moreover, synthetic chemistry may be used to introduce mutations into a polynucleotide encoding MDDT or any fragment thereof.

Embodiments of the invention can also include polynucleotides that are capable of hybridizing to the claimed polynucleotides, and, in particular, to those having the sequences shown in SEQ ID NO:57-112 and fragments thereof, under various conditions of stringency (Wahl, G.M. and S.L. Berger (1987) *Methods Enzymol.* 152:399-407; Kimmel, A.R. (1987) *Methods Enzymol.* 152:507-511). Hybridization conditions, including annealing and wash conditions, are described in "Definitions."

Methods for DNA sequencing are well known in the art and may be used to practice any of the embodiments of the invention. The methods may employ such enzymes as the Klenow fragment of DNA polymerase I, SEQUENASE (US Biochemical, Cleveland OH), Taq polymerase (Applied Biosystems), thermostable T7 polymerase (Amersham Biosciences, Piscataway NJ), or combinations of polymerases and proofreading exonucleases such as those found in the ELONGASE amplification system (Invitrogen, Carlsbad CA). Preferably, sequence preparation is automated with machines such as the MICROLAB 2200 liquid transfer system (Hamilton, Reno NV), PTC200 thermal cycler (MJ Research, Watertown MA) and ABI CATALYST 800 thermal cycler (Applied Biosystems). Sequencing is then carried out using either the ABI 373 or 377 DNA sequencing system (Applied Biosystems), the MEGABACE 1000 DNA sequencing system (Amersham Biosciences), or other systems known in the art. The resulting sequences are analyzed using a variety of algorithms which are well known in the art (Ausubel et al., *supra*, ch. 7; Meyers, R.A. (1995) Molecular Biology and

Biotechnology, Wiley VCH, New York NY, pp. 856-853).

The nucleic acids encoding MDDT may be extended utilizing a partial nucleotide sequence and employing various PCR-based methods known in the art to detect upstream sequences, such as promoters and regulatory elements. For example, one method which may be employed,

5 restriction-site PCR, uses universal and nested primers to amplify unknown sequence from genomic DNA within a cloning vector (Sarkar, G. (1993) PCR Methods Applic. 2:318-322). Another method, inverse PCR, uses primers that extend in divergent directions to amplify unknown sequence from a circularized template. The template is derived from restriction fragments comprising a known genomic locus and surrounding sequences (Triglia, T. et al. (1988) Nucleic Acids Res. 16:8186). A

10 third method, capture PCR, involves PCR amplification of DNA fragments adjacent to known sequences in human and yeast artificial chromosome DNA (Lagerstrom, M. et al. (1991) PCR Methods Applic. 1:111-119). In this method, multiple restriction enzyme digestions and ligations may be used to insert an engineered double-stranded sequence into a region of unknown sequence before performing PCR. Other methods which may be used to retrieve unknown sequences are

15 known in the art (Parker, J.D. et al. (1991) Nucleic Acids Res. 19:3055-3060). Additionally, one may use PCR, nested primers, and PROMOTERFINDER libraries (Clontech, Palo Alto CA) to walk genomic DNA. This procedure avoids the need to screen libraries and is useful in finding intron/exon junctions. For all PCR-based methods, primers may be designed using commercially available software, such as OLIGO 4.06 primer analysis software (National Biosciences, Plymouth MN) or

20 another appropriate program, to be about 22 to 30 nucleotides in length, to have a GC content of about 50% or more, and to anneal to the template at temperatures of about 68°C to 72°C.

When screening for full length cDNAs, it is preferable to use libraries that have been size-selected to include larger cDNAs. In addition, random-primed libraries, which often include sequences containing the 5' regions of genes, are preferable for situations in which an oligo d(T)

25 library does not yield a full-length cDNA. Genomic libraries may be useful for extension of sequence into 5' non-transcribed regulatory regions.

Capillary electrophoresis systems which are commercially available may be used to analyze the size or confirm the nucleotide sequence of sequencing or PCR products. In particular, capillary sequencing may employ flowable polymers for electrophoretic separation, four different nucleotide-specific, laser-stimulated fluorescent dyes, and a charge coupled device camera for detection of the

30 emitted wavelengths. Output/light intensity may be converted to electrical signal using appropriate software (e.g., GENOTYPER and SEQUENCE NAVIGATOR, Applied Biosystems), and the entire process from loading of samples to computer analysis and electronic data display may be computer controlled. Capillary electrophoresis is especially preferable for sequencing small DNA fragments

35 which may be present in limited amounts in a particular sample.

In another embodiment of the invention, polynucleotides or fragments thereof which encode MDDT may be cloned in recombinant DNA molecules that direct expression of MDDT, or fragments or functional equivalents thereof, in appropriate host cells. Due to the inherent degeneracy of the genetic code, other polynucleotides which encode substantially the same or a functionally equivalent polypeptides may be produced and used to express MDDT.

The polynucleotides of the invention can be engineered using methods generally known in the art in order to alter MDDT-encoding sequences for a variety of purposes including, but not limited to, modification of the cloning, processing, and/or expression of the gene product. DNA shuffling by random fragmentation and PCR reassembly of gene fragments and synthetic oligonucleotides may be used to engineer the nucleotide sequences. For example, oligonucleotide-mediated site-directed mutagenesis may be used to introduce mutations that create new restriction sites, alter glycosylation patterns, change codon preference, produce splice variants, and so forth.

The nucleotides of the present invention may be subjected to DNA shuffling techniques such as MOLECULARBREEDING (Maxygen Inc., Santa Clara CA; described in U.S. Patent No. 5,837,458; Chang, C.-C. et al. (1999) Nat. Biotechnol. 17:793-797; Christians, F.C. et al. (1999) Nat. Biotechnol. 17:259-264; and Crameri, A. et al. (1996) Nat. Biotechnol. 14:315-319) to alter or improve the biological properties of MDDT, such as its biological or enzymatic activity or its ability to bind to other molecules or compounds. DNA shuffling is a process by which a library of gene variants is produced using PCR-mediated recombination of gene fragments. The library is then subjected to selection or screening procedures that identify those gene variants with the desired properties. These preferred variants may then be pooled and further subjected to recursive rounds of DNA shuffling and selection/screening. Thus, genetic diversity is created through "artificial" breeding and rapid molecular evolution. For example, fragments of a single gene containing random point mutations may be recombined, screened, and then reshuffled until the desired properties are optimized. Alternatively, fragments of a given gene may be recombined with fragments of homologous genes in the same gene family, either from the same or different species, thereby maximizing the genetic diversity of multiple naturally occurring genes in a directed and controllable manner.

In another embodiment, polynucleotides encoding MDDT may be synthesized, in whole or in part, using one or more chemical methods well known in the art (Caruthers, M.H. et al. (1980) Nucleic Acids Symp. Ser. 7:215-223; Horn, T. et al. (1980) Nucleic Acids Symp. Ser. 7:225-232). Alternatively, MDDT itself or a fragment thereof may be synthesized using chemical methods known in the art. For example, peptide synthesis can be performed using various solution-phase or solid-phase techniques (Creighton, T. (1984) Proteins, Structures and Molecular Properties, WH Freeman, New York NY, pp. 55-60; Roberge, J.Y. et al. (1995) Science 269:202-204). Automated

synthesis may be achieved using the ABI 431A peptide synthesizer (Applied Biosystems). Additionally, the amino acid sequence of MDDT, or any part thereof, may be altered during direct synthesis and/or combined with sequences from other proteins, or any part thereof, to produce a variant polypeptide or a polypeptide having a sequence of a naturally occurring polypeptide.

5       The peptide may be substantially purified by preparative high performance liquid chromatography (Chiez, R.M. and F.Z. Regnier (1990) *Methods Enzymol.* 182:392-421). The composition of the synthetic peptides may be confirmed by amino acid analysis or by sequencing. (Creighton, *supra*, pp. 28-53).

10       In order to express a biologically active MDDT, the polynucleotides encoding MDDT or derivatives thereof may be inserted into an appropriate expression vector, i.e., a vector which contains the necessary elements for transcriptional and translational control of the inserted coding sequence in a suitable host. These elements include regulatory sequences, such as enhancers, constitutive and inducible promoters, and 5' and 3' untranslated regions in the vector and in polynucleotides encoding MDDT. Such elements may vary in their strength and specificity. Specific initiation signals may also  
15       be used to achieve more efficient translation of polynucleotides encoding MDDT. Such signals include the ATG initiation codon and adjacent sequences, e.g. the Kozak sequence. In cases where a polynucleotide sequence encoding MDDT and its initiation codon and upstream regulatory sequences are inserted into the appropriate expression vector, no additional transcriptional or translational control signals may be needed. However, in cases where only coding sequence, or a fragment  
20       thereof, is inserted, exogenous translational control signals including an in-frame ATG initiation codon should be provided by the vector. Exogenous translational elements and initiation codons may be of various origins, both natural and synthetic. The efficiency of expression may be enhanced by the inclusion of enhancers appropriate for the particular host cell system used (Scharf, D. et al. (1994) *Results Probl. Cell Differ.* 20:125-162).

25       Methods which are well known to those skilled in the art may be used to construct expression vectors containing polynucleotides encoding MDDT and appropriate transcriptional and translational control elements. These methods include *in vitro* recombinant DNA techniques, synthetic techniques, and *in vivo* genetic recombination (Sambrook, J. et al. (1989) Molecular Cloning, A Laboratory Manual, Cold Spring Harbor Press, Plainview NY, ch. 4, 8, and 16-17; Ausubel et al., *supra*, ch. 1, 3,  
30       and 15).

      A variety of expression vector/host systems may be utilized to contain and express polynucleotides encoding MDDT. These include, but are not limited to, microorganisms such as bacteria transformed with recombinant bacteriophage, plasmid, or cosmid DNA expression vectors; yeast transformed with yeast expression vectors; insect cell systems infected with viral expression  
35       vectors (e.g., baculovirus); plant cell systems transformed with viral expression vectors (e.g.,

cauliflower mosaic virus, CaMV, or tobacco mosaic virus, TMV) or with bacterial expression vectors (e.g., Ti or pBR322 plasmids); or animal cell systems (Sambrook, *supra*; Ausubel et al., *supra*; Van Heeke, G. and S.M. Schuster (1989) J. Biol. Chem. 264:5503-5509; Engelhard, E.K. et al. (1994) Proc. Natl. Acad. Sci. USA 91:3224-3227; Sandig, V. et al. (1996) Hum. Gene Ther. 7:1937-1945; Takamatsu, N. (1987) EMBO J. 6:307-311; The McGraw Hill Yearbook of Science and Technology (1992) McGraw Hill, New York NY, pp. 191-196; Logan, J. and T. Shenk (1984) Proc. Natl. Acad. Sci. USA 81:3655-3659; Harrington, J.J. et al. (1997) Nat. Genet. 15:345-355). Expression vectors derived from retroviruses, adenoviruses, or herpes or vaccinia viruses, or from various bacterial plasmids, may be used for delivery of polynucleotides to the targeted organ, tissue, or cell population (Di Nicola, M. et al. (1998) Cancer Gen. Ther. 5:350-356; Yu, M. et al. (1993) Proc. Natl. Acad. Sci. USA 90:6340-6344; Buller, R.M. et al. (1985) Nature 317:813-815; McGregor, D.P. et al. (1994) Mol. Immunol. 31:219-226; Verma, I.M. and N. Somia (1997) Nature 389:239-242). The invention is not limited by the host cell employed.

In bacterial systems, a number of cloning and expression vectors may be selected depending upon the use intended for polynucleotides encoding MDDT. For example, routine cloning, subcloning, and propagation of polynucleotides encoding MDDT can be achieved using a multifunctional *E. coli* vector such as PBLUESCRIPT (Stratagene, La Jolla CA) or PSPORT1 plasmid (Invitrogen). Ligation of polynucleotides encoding MDDT into the vector's multiple cloning site disrupts the *lacZ* gene, allowing a colorimetric screening procedure for identification of transformed bacteria containing recombinant molecules. In addition, these vectors may be useful for *in vitro* transcription, dideoxy sequencing, single strand rescue with helper phage, and creation of nested deletions in the cloned sequence (Van Heeke, G. and S.M. Schuster (1989) J. Biol. Chem. 264:5503-5509). When large quantities of MDDT are needed, e.g. for the production of antibodies, vectors which direct high level expression of MDDT may be used. For example, vectors containing the strong, inducible SP6 or T7 bacteriophage promoter may be used.

Yeast expression systems may be used for production of MDDT. A number of vectors containing constitutive or inducible promoters, such as alpha factor, alcohol oxidase, and PGH promoters, may be used in the yeast *Saccharomyces cerevisiae* or *Pichia pastoris*. In addition, such vectors direct either the secretion or intracellular retention of expressed proteins and enable integration of foreign polynucleotide sequences into the host genome for stable propagation (Ausubel et al., *supra*; Bitter, G.A. et al. (1987) Methods Enzymol. 153:516-544; Scorer, C.A. et al. (1994) Bio/Technology 12:181-184).

Plant systems may also be used for expression of MDDT. Transcription of polynucleotides encoding MDDT may be driven by viral promoters, e.g., the 35S and 19S promoters of CaMV used alone or in combination with the omega leader sequence from TMV (Takamatsu, N. (1987) EMBO J.

6:307-311). Alternatively, plant promoters such as the small subunit of RUBISCO or heat shock promoters may be used (Coruzzi, G. et al. (1984) EMBO J. 3:1671-1680; Broglie, R. et al. (1984) Science 224:838-843; Winter, J. et al. (1991) Results Probl. Cell Differ. 17:85-105). These constructs can be introduced into plant cells by direct DNA transformation or pathogen-mediated transfection (The McGraw Hill Yearbook of Science and Technology (1992) McGraw Hill, New York NY, pp. 191-196).

In mammalian cells, a number of viral-based expression systems may be utilized. In cases where an adenovirus is used as an expression vector, polynucleotides encoding MDDT may be ligated into an adenovirus transcription/translation complex consisting of the late promoter and tripartite leader sequence. Insertion in a non-essential E1 or E3 region of the viral genome may be used to obtain infective virus which expresses MDDT in host cells (Logan, J. and T. Shenk (1984) Proc. Natl. Acad. Sci. USA 81:3655-3659). In addition, transcription enhancers, such as the Rous sarcoma virus (RSV) enhancer, may be used to increase expression in mammalian host cells. SV40 or EBV-based vectors may also be used for high-level protein expression.

Human artificial chromosomes (HACs) may also be employed to deliver larger fragments of DNA than can be contained in and expressed from a plasmid. HACs of about 6 kb to 10 Mb are constructed and delivered via conventional delivery methods (liposomes, polycationic amino polymers, or vesicles) for therapeutic purposes (Harrington, J.J. et al. (1997) Nat. Genet. 15:345-355).

For long term production of recombinant proteins in mammalian systems, stable expression of MDDT in cell lines is preferred. For example, polynucleotides encoding MDDT can be transformed into cell lines using expression vectors which may contain viral origins of replication and/or endogenous expression elements and a selectable marker gene on the same or on a separate vector. Following the introduction of the vector, cells may be allowed to grow for about 1 to 2 days in enriched media before being switched to selective media. The purpose of the selectable marker is to confer resistance to a selective agent, and its presence allows growth and recovery of cells which successfully express the introduced sequences. Resistant clones of stably transformed cells may be propagated using tissue culture techniques appropriate to the cell type.

Any number of selection systems may be used to recover transformed cell lines. These include, but are not limited to, the herpes simplex virus thymidine kinase and adenine phosphoribosyltransferase genes, for use in *tk* and *ap<sup>r</sup>* cells, respectively (Wigler, M. et al. (1977) Cell 11:223-232; Lowy, I. et al. (1980) Cell 22:817-823). Also, antimetabolite, antibiotic, or herbicide resistance can be used as the basis for selection. For example, *dhfr* confers resistance to methotrexate; *neo* confers resistance to the aminoglycosides neomycin and G-418; and *als* and *pat* confer resistance to chlorsulfuron and phosphinotricin acetyltransferase, respectively (Wigler, M. et al. (1980) Proc. Natl. Acad. Sci. USA 77:3567-3570; Colbere-Garapin, F. et al. (1981) J. Mol. Biol.



150:1-14). Additional selectable genes have been described, e.g., *trpB* and *hisD*, which alter cellular requirements for metabolites (Hartman, S.C. and R.C. Mulligan (1988) Proc. Natl. Acad. Sci. USA 85:8047-8051). Visible markers, e.g., anthocyanins, green fluorescent proteins (GFP; Clontech),  $\beta$ -glucuronidase and its substrate  $\beta$ -glucuronide, or luciferase and its substrate luciferin may be used.

- 5 These markers can be used not only to identify transformants, but also to quantify the amount of transient or stable protein expression attributable to a specific vector system (Rhodes, C.A. (1995) Methods Mol. Biol. 55:121-131).

Although the presence/absence of marker gene expression suggests that the gene of interest is also present, the presence and expression of the gene may need to be confirmed. For example, if the  
10 sequence encoding MDDT is inserted within a marker gene sequence, transformed cells containing polynucleotides encoding MDDT can be identified by the absence of marker gene function. Alternatively, a marker gene can be placed in tandem with a sequence encoding MDDT under the control of a single promoter. Expression of the marker gene in response to induction or selection usually indicates expression of the tandem gene as well.

- 15 In general, host cells that contain the polynucleotide encoding MDDT and that express MDDT may be identified by a variety of procedures known to those of skill in the art. These procedures include, but are not limited to, DNA-DNA or DNA-RNA hybridizations, PCR amplification, and protein bioassay or immunoassay techniques which include membrane, solution, or chip based technologies for the detection and/or quantification of nucleic acid or protein sequences.

- 20 Immunological methods for detecting and measuring the expression of MDDT using either specific polyclonal or monoclonal antibodies are known in the art. Examples of such techniques include enzyme-linked immunosorbent assays (ELISAs), radioimmunoassays (RIAs), and fluorescence activated cell sorting (FACS). A two-site, monoclonal-based immunoassay utilizing monoclonal antibodies reactive to two non-interfering epitopes on MDDT is preferred, but a  
25 competitive binding assay may be employed. These and other assays are well known in the art (Hampton, R. et al. (1990) Serological Methods, a Laboratory Manual, APS Press, St. Paul MN, Sect. IV; Coligan, J.E. et al. (1997) Current Protocols in Immunology, Greene Pub. Associates and Wiley-Interscience, New York NY; Pound, J.D. (1998) Immunochemical Protocols, Humana Press, Totowa NJ).

- 30 A wide variety of labels and conjugation techniques are known by those skilled in the art and may be used in various nucleic acid and amino acid assays. Means for producing labeled hybridization or PCR probes for detecting sequences related to polynucleotides encoding MDDT include oligolabeling, nick translation, end-labeling, or PCR amplification using a labeled nucleotide. Alternatively, polynucleotides encoding MDDT, or any fragments thereof, may be cloned into a  
35 vector for the production of an mRNA probe. Such vectors are known in the art, are commercially

available, and may be used to synthesize RNA probes *in vitro* by addition of an appropriate RNA polymerase such as T7, T3, or SP6 and labeled nucleotides. These procedures may be conducted using a variety of commercially available kits, such as those provided by Amersham Biosciences, Promega (Madison WI), and US Biochemical. Suitable reporter molecules or labels which may be  
5 used for ease of detection include radionuclides, enzymes, fluorescent, chemiluminescent, or chromogenic agents, as well as substrates, cofactors, inhibitors, magnetic particles, and the like.

Host cells transformed with polynucleotides encoding MDDT may be cultured under conditions suitable for the expression and recovery of the protein from cell culture. The protein produced by a transformed cell may be secreted or retained intracellularly depending on the sequence  
10 and/or the vector used. As will be understood by those of skill in the art, expression vectors containing polynucleotides which encode MDDT may be designed to contain signal sequences which direct secretion of MDDT through a prokaryotic or eukaryotic cell membrane.

In addition, a host cell strain may be chosen for its ability to modulate expression of the inserted polynucleotides or to process the expressed protein in the desired fashion. Such  
15 modifications of the polypeptide include, but are not limited to, acetylation, carboxylation, glycosylation, phosphorylation, lipidation, and acylation. Post-translational processing which cleaves a "prepro" or "pro" form of the protein may also be used to specify protein targeting, folding, and/or activity. Different host cells which have specific cellular machinery and characteristic mechanisms for post-translational activities (e.g., CHO, HeLa, MDCK, HEK293, and WI38) are available from the  
20 American Type Culture Collection (ATCC, Manassas VA) and may be chosen to ensure the correct modification and processing of the foreign protein.

In another embodiment of the invention, natural, modified, or recombinant polynucleotides encoding MDDT may be ligated to a heterologous sequence resulting in translation of a fusion protein in any of the aforementioned host systems. For example, a chimeric MDDT protein  
25 containing a heterologous moiety that can be recognized by a commercially available antibody may facilitate the screening of peptide libraries for inhibitors of MDDT activity. Heterologous protein and peptide moieties may also facilitate purification of fusion proteins using commercially available affinity matrices. Such moieties include, but are not limited to, glutathione S-transferase (GST), maltose binding protein (MBP), thioredoxin (Trx), calmodulin binding peptide (CBP), 6-His, FLAG,  
30 *c-myc*, and hemagglutinin (HA). GST, MBP, Trx, CBP, and 6-His enable purification of their cognate fusion proteins on immobilized glutathione, maltose, phenylarsine oxide, calmodulin, and metal-chelate resins, respectively. FLAG, *c-myc*, and hemagglutinin (HA) enable immunoaffinity purification of fusion proteins using commercially available monoclonal and polyclonal antibodies that specifically recognize these epitope tags. A fusion protein may also be engineered to contain a  
35 proteolytic cleavage site located between the MDDT encoding sequence and the heterologous protein

sequence, so that MDDT may be cleaved away from the heterologous moiety following purification. Methods for fusion protein expression and purification are discussed in Ausubel et al. (*supra*, ch. 10 and 16). A variety of commercially available kits may also be used to facilitate expression and purification of fusion proteins.

5 In another embodiment, synthesis of radiolabeled MDDT may be achieved *in vitro* using the TNT rabbit reticulocyte lysate or wheat germ extract system (Promega). These systems couple transcription and translation of protein-coding sequences operably associated with the T7, T3, or SP6 promoters. Translation takes place in the presence of a radiolabeled amino acid precursor, for example, <sup>35</sup>S-methionine.

10 MDDT, fragments of MDDT, or variants of MDDT may be used to screen for compounds that specifically bind to MDDT. One or more test compounds may be screened for specific binding to MDDT. In various embodiments, 1, 2, 3, 4, 5, 10, 20, 50, 100, or 200 test compounds can be screened for specific binding to MDDT. Examples of test compounds can include antibodies, anticalins, oligonucleotides, proteins (e.g., ligands or receptors), or small molecules.

15 In related embodiments, variants of MDDT can be used to screen for binding of test compounds, such as antibodies, to MDDT, a variant of MDDT, or a combination of MDDT and/or one or more variants MDDT. In an embodiment, a variant of MDDT can be used to screen for compounds that bind to a variant of MDDT, but not to MDDT having the exact sequence of a sequence of SEQ ID NO:1-56. MDDT variants used to perform such screening can have a range of  
20 about 50% to about 99% sequence identity to MDDT, with various embodiments having 60%, 70%, 75%, 80%, 85%, 90%, and 95% sequence identity.

In an embodiment, a compound identified in a screen for specific binding to MDDT can be closely related to the natural ligand of MDDT, e.g., a ligand or fragment thereof, a natural substrate, a structural or functional mimetic, or a natural binding partner (Coligan, J.E. et al. (1991) Current  
25 Protocols in Immunology 1(2):Chapter 5). In another embodiment, the compound thus identified can be a natural ligand of a receptor MDDT (Howard, A.D. et al. (2001) Trends Pharmacol. Sci.22:132-140; Wise, A. et al. (2002) Drug Discovery Today 7:235-246).

In other embodiments, a compound identified in a screen for specific binding to MDDT can be closely related to the natural receptor to which MDDT binds, at least a fragment of the receptor, or  
30 a fragment of the receptor including all or a portion of the ligand binding site or binding pocket. For example, the compound may be a receptor for MDDT which is capable of propagating a signal, or a decoy receptor for MDDT which is not capable of propagating a signal (Ashkenazi, A. and V.M. Divit (1999) Curr. Opin. Cell Biol. 11:255-260; Mantovani, A. et al. (2001) Trends Immunol. 22:328-336). The compound can be rationally designed using known techniques. Examples of such  
35 techniques include those used to construct the compound etanercept (ENBREL; Immunex Corp.,

Seattle WA), which is efficacious for treating rheumatoid arthritis in humans. Etanercept is an engineered p75 tumor necrosis factor (TNF) receptor dimer linked to the Fc portion of human IgG<sub>1</sub> (Taylor, P.C. et al. (2001) Curr. Opin. Immunol. 13:611-616).

In one embodiment, two or more antibodies having similar or, alternatively, different specificities can be screened for specific binding to MDDT, fragments of MDDT, or variants of MDDT. The binding specificity of the antibodies thus screened can thereby be selected to identify particular fragments or variants of MDDT. In one embodiment, an antibody can be selected such that its binding specificity allows for preferential identification of specific fragments or variants of MDDT. In another embodiment, an antibody can be selected such that its binding specificity allows for preferential diagnosis of a specific disease or condition having increased, decreased, or otherwise abnormal production of MDDT.

In an embodiment, anticalins can be screened for specific binding to MDDT, fragments of MDDT, or variants of MDDT. Anticalins are ligand-binding proteins that have been constructed based on a lipocalin scaffold (Weiss, G.A. and H.B. Lowman (2000) Chem. Biol. 7:R177-R184; Skerra, A. (2001) J. Biotechnol. 74:257-275). The protein architecture of lipocalins can include a beta-barrel having eight antiparallel beta-strands, which supports four loops at its open end. These loops form the natural ligand-binding site of the lipocalins, a site which can be re-engineered *in vitro* by amino acid substitutions to impart novel binding specificities. The amino acid substitutions can be made using methods known in the art or described herein, and can include conservative substitutions (e.g., substitutions that do not alter binding specificity) or substitutions that modestly, moderately, or significantly alter binding specificity.

In one embodiment, screening for compounds which specifically bind to, stimulate, or inhibit MDDT involves producing appropriate cells which express MDDT, either as a secreted protein or on the cell membrane. Preferred cells include cells from mammals, yeast, *Drosophila*, or *E. coli*. Cells expressing MDDT or cell membrane fractions which contain MDDT are then contacted with a test compound and binding, stimulation, or inhibition of activity of either MDDT or the compound is analyzed.

An assay may simply test binding of a test compound to the polypeptide, wherein binding is detected by a fluorophore, radioisotope, enzyme conjugate, or other detectable label. For example, the assay may comprise the steps of combining at least one test compound with MDDT, either in solution or affixed to a solid support, and detecting the binding of MDDT to the compound. Alternatively, the assay may detect or measure binding of a test compound in the presence of a labeled competitor. Additionally, the assay may be carried out using cell-free preparations, chemical libraries, or natural product mixtures, and the test compound(s) may be free in solution or affixed to a solid support.

An assay can be used to assess the ability of a compound to bind to its natural ligand and/or to inhibit the binding of its natural ligand to its natural receptors. Examples of such assays include radio-labeling assays such as those described in U.S. Patent No. 5,914,236 and U.S. Patent No. 6,372,724. In a related embodiment, one or more amino acid substitutions can be introduced into a polypeptide compound (such as a receptor) to improve or alter its ability to bind to its natural ligands (Matthews, D.J. and J.A. Wells. (1994) Chem. Biol. 1:25-30). In another related embodiment, one or more amino acid substitutions can be introduced into a polypeptide compound (such as a ligand) to improve or alter its ability to bind to its natural receptors (Cunningham, B.C. and J.A. Wells (1991) Proc. Natl. Acad. Sci. USA 88:3407-3411; Lowman, H.B. et al. (1991) J. Biol. Chem. 266:10982-10988).

MDDT, fragments of MDDT, or variants of MDDT may be used to screen for compounds that modulate the activity of MDDT. Such compounds may include agonists, antagonists, or partial or inverse agonists. In one embodiment, an assay is performed under conditions permissive for MDDT activity, wherein MDDT is combined with at least one test compound, and the activity of MDDT in the presence of a test compound is compared with the activity of MDDT in the absence of the test compound. A change in the activity of MDDT in the presence of the test compound is indicative of a compound that modulates the activity of MDDT. Alternatively, a test compound is combined with an *in vitro* or cell-free system comprising MDDT under conditions suitable for MDDT activity, and the assay is performed. In either of these assays, a test compound which modulates the activity of MDDT may do so indirectly and need not come in direct contact with the test compound. At least one and up to a plurality of test compounds may be screened.

In another embodiment, polynucleotides encoding MDDT or their mammalian homologs may be "knocked out" in an animal model system using homologous recombination in embryonic stem (ES) cells. Such techniques are well known in the art and are useful for the generation of animal models of human disease (see, e.g., U.S. Patent No. 5,175,383 and U.S. Patent No. 5,767,337). For example, mouse ES cells, such as the mouse 129/SvJ cell line, are derived from the early mouse embryo and grown in culture. The ES cells are transformed with a vector containing the gene of interest disrupted by a marker gene, e.g., the neomycin phosphotransferase gene (*neo*; Capecchi, M.R. (1989) Science 244:1288-1292). The vector integrates into the corresponding region of the host genome by homologous recombination. Alternatively, homologous recombination takes place using the Cre-loxP system to knockout a gene of interest in a tissue- or developmental stage-specific manner (Marth, J.D. (1996) Clin. Invest. 97:1999-2002; Wagner, K.U. et al. (1997) Nucleic Acids Res. 25:4323-4330). Transformed ES cells are identified and microinjected into mouse cell blastocysts such as those from the C57BL/6 mouse strain. The blastocysts are surgically transferred to pseudopregnant dams, and the resulting chimeric progeny are genotyped and bred to produce

heterozygous or homozygous strains. Transgenic animals thus generated may be tested with potential therapeutic or toxic agents.

Polynucleotides encoding MDDT may also be manipulated *in vitro* in ES cells derived from human blastocysts. Human ES cells have the potential to differentiate into at least eight separate cell lineages including endoderm, mesoderm, and ectodermal cell types. These cell lineages differentiate into, for example, neural cells, hematopoietic lineages, and cardiomyocytes (Thomson, J.A. et al. (1998) Science 282:1145-1147).

Polynucleotides encoding MDDT can also be used to create "knockin" humanized animals (pigs) or transgenic animals (mice or rats) to model human disease. With knockin technology, a region of a polynucleotide encoding MDDT is injected into animal ES cells, and the injected sequence integrates into the animal cell genome. Transformed cells are injected into blastulae, and the blastulae are implanted as described above. Transgenic progeny or inbred lines are studied and treated with potential pharmaceutical agents to obtain information on treatment of a human disease. Alternatively, a mammal inbred to overexpress MDDT, e.g., by secreting MDDT in its milk, may also serve as a convenient source of that protein (Janne, J. et al. (1998) Biotechnol. Annu. Rev. 4:55-74).

#### THERAPEUTICS

Chemical and structural similarity, e.g., in the context of sequences and motifs, exists between regions of MDDT and molecules for disease detection and treatment. In particular, SEQ ID NO:110 shows co-expression with osteoporosis-relevant genes. In addition, examples of tissues expressing MDDT can be found in Table 6 and can also be found in Example XI. Therefore, MDDT appears to play a role in cell proliferative, autoimmune/inflammatory, developmental, and neurological disorders, diseases treated with steroids and disorders caused by the metabolic response to treatment with steroids. In the treatment of disorders associated with increased MDDT expression or activity, it is desirable to decrease the expression or activity of MDDT. In the treatment of disorders associated with decreased MDDT expression or activity, it is desirable to increase the expression or activity of MDDT.

Therefore, in one embodiment, MDDT or a fragment or derivative thereof may be administered to a subject to treat or prevent a disorder associated with decreased expression or activity of MDDT. Examples of such disorders include, but are not limited to, a cell proliferative disorder such as actinic keratosis, arteriosclerosis, atherosclerosis, bursitis, cirrhosis, hepatitis, mixed connective tissue disease (MCTD), myelofibrosis, paroxysmal nocturnal hemoglobinuria, polycythemia vera, psoriasis, primary thrombocythemia, and cancers including adenocarcinoma, leukemia, lymphoma, melanoma, myeloma, sarcoma, teratocarcinoma, and, in particular, cancers of the adrenal gland, bladder, bone, bone marrow, brain, breast, cervix, gall bladder, ganglia, gastrointestinal tract, heart, kidney, liver, lung, muscle, ovary, pancreas, parathyroid, penis, prostate,

salivary glands, skin, spleen, testis, thymus, thyroid, and uterus; an autoimmune/inflammatory disorder such as acquired immunodeficiency syndrome (AIDS), Addison's disease, adult respiratory distress syndrome, allergies, ankylosing spondylitis, amyloidosis, anemia, asthma, atherosclerosis, autoimmune hemolytic anemia, autoimmune thyroiditis, autoimmune polyendocrinopathy-

5 candidiasis-ectodermal dystrophy (APECED), bronchitis, cholecystitis, contact dermatitis, Crohn's disease, atopic dermatitis, dermatomyositis, diabetes mellitus, emphysema, episodic lymphopenia with lymphocytotoxins, erythroblastosis fetalis, erythema nodosum, atrophic gastritis, glomerulonephritis, Goodpasture's syndrome, gout, Graves' disease, Hashimoto's thyroiditis, hypereosinophilia, irritable bowel syndrome, multiple sclerosis, myasthenia gravis, myocardial or

10 pericardial inflammation, osteoarthritis, osteoporosis, pancreatitis, polymyositis, psoriasis, Reiter's syndrome, rheumatoid arthritis, scleroderma, Sjögren's syndrome, systemic anaphylaxis, systemic lupus erythematosus, systemic sclerosis, thrombocytopenic purpura, ulcerative colitis, uveitis, Werner syndrome, complications of cancer, hemodialysis, and extracorporeal circulation, viral, bacterial, fungal, parasitic, protozoal, and helminthic infections, and trauma; a disease treated with a

15 steroid and a disorder caused by the metabolic response to treatment with steroids, such as adenomatosis, cholestasis, cirrhosis, hemangioma, Henoch-Schonlein purpura, hepatitis, hepatocellular and metastatic carcinomas, idiopathic thrombocytopenic purpura, porphyria, sarcoidosis, and Wilson disease; a developmental disorder such as renal tubular acidosis, anemia, Cushing's syndrome, achondroplastic dwarfism, Duchenne and Becker muscular dystrophy, epilepsy,

20 gonadal dysgenesis, WAGR syndrome (Wilms' tumor, aniridia, genitourinary abnormalities, and mental retardation), Smith-Magenis syndrome, myelodysplastic syndrome, hereditary mucoepithelial dysplasia, hereditary keratodermas, hereditary neuropathies such as Charcot-Marie-Tooth disease and neurofibromatosis, hypothyroidism, hydrocephalus, seizure disorders such as Sydenham's chorea and cerebral palsy, spina bifida, anencephaly, craniorachischisis, congenital glaucoma, cataract, and

25 sensorineural hearing loss; and a neurological disorder such as epilepsy, ischemic cerebrovascular disease, stroke, cerebral neoplasms, Alzheimer's disease, Pick's disease, Huntington's disease, dementia, Parkinson's disease and other extrapyramidal disorders, amyotrophic lateral sclerosis and other motor neuron disorders, progressive neural muscular atrophy, retinitis pigmentosa, hereditary ataxias, multiple sclerosis and other demyelinating diseases, bacterial and viral meningitis, brain

30 abscess, subdural empyema, epidural abscess, suppurative intracranial thrombophlebitis, myelitis and radiculitis, viral central nervous system disease, prion diseases including kuru, Creutzfeldt-Jakob disease, and Gerstmann-Straussler-Scheinker syndrome, fatal familial insomnia, nutritional and metabolic diseases of the nervous system, neurofibromatosis, tuberous sclerosis, cerebelloretinal hemangioblastomatosis, encephalotrigeminal syndrome, mental retardation and other developmental

35 disorders of the central nervous system including Down syndrome, cerebral palsy, neuroskeletal

disorders, autonomic nervous system disorders, cranial nerve disorders, spinal cord diseases, muscular dystrophy and other neuromuscular disorders, peripheral nervous system disorders, dermatomyositis and polymyositis, inherited, metabolic, endocrine, and toxic myopathies, myasthenia gravis, periodic paralysis, mental disorders including mood, anxiety, and schizophrenic disorders, seasonal affective disorder (SAD), akathisia, amnesia, catatonia, diabetic neuropathy, tardive dyskinesia, dystonias, paranoid psychoses, postherpetic neuralgia, Tourette's disorder, progressive supranuclear palsy, corticobasal degeneration, and familial frontotemporal dementia. SEQ ID NO:2 can be used in the diagnosis and treatment of Tangier disease and SEQ ID NO:5 can be used in the diagnosis and treatment of type II diabetes.

10 In another embodiment, a vector capable of expressing MDDT or a fragment or derivative thereof may be administered to a subject to treat or prevent a disorder associated with decreased expression or activity of MDDT including, but not limited to, those described above.

In a further embodiment, a composition comprising a substantially purified MDDT in conjunction with a suitable pharmaceutical carrier may be administered to a subject to treat or prevent a disorder associated with decreased expression or activity of MDDT including, but not limited to, those provided above.

In still another embodiment, an agonist which modulates the activity of MDDT may be administered to a subject to treat or prevent a disorder associated with decreased expression or activity of MDDT including, but not limited to, those listed above.

20 In a further embodiment, an antagonist of MDDT may be administered to a subject to treat or prevent a disorder associated with increased expression or activity of MDDT. Examples of such disorders include, but are not limited to, those cell proliferative, autoimmune/inflammatory, developmental, and neurological disorders, diseases treated with steroids and disorders caused by the metabolic response to treatment with steroids described above. In one aspect, an antibody which specifically binds MDDT may be used directly as an antagonist or indirectly as a targeting or delivery mechanism for bringing a pharmaceutical agent to cells or tissues which express MDDT.

In an additional embodiment, a vector expressing the complement of the polynucleotide encoding MDDT may be administered to a subject to treat or prevent a disorder associated with increased expression or activity of MDDT including, but not limited to, those described above.

30 In other embodiments, any protein, agonist, antagonist, antibody, complementary sequence, or vector embodiments may be administered in combination with other appropriate therapeutic agents. Selection of the appropriate agents for use in combination therapy may be made by one of ordinary skill in the art, according to conventional pharmaceutical principles. The combination of therapeutic agents may act synergistically to effect the treatment or prevention of the various disorders described above. Using this approach, one may be able to achieve therapeutic efficacy with



lower dosages of each agent, thus reducing the potential for adverse side effects.

An antagonist of MDDT may be produced using methods which are generally known in the art. In particular, purified MDDT may be used to produce antibodies or to screen libraries of pharmaceutical agents to identify those which specifically bind MDDT. Antibodies to MDDT may also be generated using methods that are well known in the art. Such antibodies may include, but are not limited to, polyclonal, monoclonal, chimeric, and single chain antibodies, Fab fragments, and fragments produced by a Fab expression library. Neutralizing antibodies (i.e., those which inhibit dimer formation) are generally preferred for therapeutic use. Single chain antibodies (e.g., from camels or llamas) may be potent enzyme inhibitors and may have advantages in the design of peptide mimetics, and in the development of immuno-adsorbents and biosensors (Muyldermans, S. (2001) J. Biotechnol. 74:277-302).

For the production of antibodies, various hosts including goats, rabbits, rats, mice, camels, dromedaries, llamas, humans, and others may be immunized by injection with MDDT or with any fragment or oligopeptide thereof which has immunogenic properties. Depending on the host species, various adjuvants may be used to increase immunological response. Such adjuvants include, but are not limited to, Freund's, mineral gels such as aluminum hydroxide, and surface active substances such as lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions, KLH, and dinitrophenol. Among adjuvants used in humans, BCG (bacilli Calmette-Guerin) and *Corynebacterium parvum* are especially preferable.

It is preferred that the oligopeptides, peptides, or fragments used to induce antibodies to MDDT have an amino acid sequence consisting of at least about 5 amino acids, and generally will consist of at least about 10 amino acids. It is also preferable that these oligopeptides, peptides, or fragments are identical to a portion of the amino acid sequence of the natural protein. Short stretches of MDDT amino acids may be fused with those of another protein, such as KLH, and antibodies to the chimeric molecule may be produced.

Monoclonal antibodies to MDDT may be prepared using any technique which provides for the production of antibody molecules by continuous cell lines in culture. These include, but are not limited to, the hybridoma technique, the human B-cell hybridoma technique, and the EBV-hybridoma technique (Kohler, G. et al. (1975) Nature 256:495-497; Kozbor, D. et al. (1985) J. Immunol. Methods 81:31-42; Cote, R.J. et al. (1983) Proc. Natl. Acad. Sci. USA 80:2026-2030; Cole, S.P. et al. (1984) Mol. Cell Biol. 62:109-120).

In addition, techniques developed for the production of "chimeric antibodies," such as the splicing of mouse antibody genes to human antibody genes to obtain a molecule with appropriate antigen specificity and biological activity, can be used (Morrison, S.L. et al. (1984) Proc. Natl. Acad. Sci. USA 81:6851-6855; Neuberger, M.S. et al. (1984) Nature 312:604-608; Takeda, S. et al. (1985)

Nature 314:452-454). Alternatively, techniques described for the production of single chain antibodies may be adapted, using methods known in the art, to produce MDDT-specific single chain antibodies. Antibodies with related specificity, but of distinct idiotypic composition, may be generated by chain shuffling from random combinatorial immunoglobulin libraries (Burton, D.R.

5 (1991) Proc. Natl. Acad. Sci. USA 88:10134-10137).

Antibodies may also be produced by inducing *in vivo* production in the lymphocyte population or by screening immunoglobulin libraries or panels of highly specific binding reagents as disclosed in the literature (Orlandi, R. et al. (1989) Proc. Natl. Acad. Sci. USA 86:3833-3837; Winter, G. et al. (1991) Nature 349:293-299).

10 Antibody fragments which contain specific binding sites for MDDT may also be generated. For example, such fragments include, but are not limited to,  $F(ab')_2$  fragments produced by pepsin digestion of the antibody molecule and Fab fragments generated by reducing the disulfide bridges of the  $F(ab')_2$  fragments. Alternatively, Fab expression libraries may be constructed to allow rapid and easy identification of monoclonal Fab fragments with the desired specificity (Huse, W.D. et al. (1989)  
15 Science 246:1275-1281).

Various immunoassays may be used for screening to identify antibodies having the desired specificity. Numerous protocols for competitive binding or immunoradiometric assays using either polyclonal or monoclonal antibodies with established specificities are well known in the art. Such immunoassays typically involve the measurement of complex formation between MDDT and its  
20 specific antibody. A two-site, monoclonal-based immunoassay utilizing monoclonal antibodies reactive to two non-interfering MDDT epitopes is generally used, but a competitive binding assay may also be employed (Pound, *supra*).

Various methods such as Scatchard analysis in conjunction with radioimmunoassay techniques may be used to assess the affinity of antibodies for MDDT. Affinity is expressed as an  
25 association constant,  $K_a$ , which is defined as the molar concentration of MDDT-antibody complex divided by the molar concentrations of free antigen and free antibody under equilibrium conditions. The  $K_a$  determined for a preparation of polyclonal antibodies, which are heterogeneous in their affinities for multiple MDDT epitopes, represents the average affinity, or avidity, of the antibodies for MDDT. The  $K_a$  determined for a preparation of monoclonal antibodies, which are monospecific for a  
30 particular MDDT epitope, represents a true measure of affinity. High-affinity antibody preparations with  $K_a$  ranging from about  $10^9$  to  $10^{12}$  L/mole are preferred for use in immunoassays in which the MDDT-antibody complex must withstand rigorous manipulations. Low-affinity antibody preparations with  $K_a$  ranging from about  $10^6$  to  $10^7$  L/mole are preferred for use in immunopurification and similar procedures which ultimately require dissociation of MDDT,  
35 preferably in active form, from the antibody (Catty, D. (1988) Antibodies, Volume I: A Practical

Approach, IRL Press, Washington DC; Liddell, J.E. and A. Cryer (1991) A Practical Guide to Monoclonal Antibodies, John Wiley & Sons, New York NY).

The titer and avidity of polyclonal antibody preparations may be further evaluated to determine the quality and suitability of such preparations for certain downstream applications. For example, a polyclonal antibody preparation containing at least 1-2 mg specific antibody/ml, preferably 5-10 mg specific antibody/ml, is generally employed in procedures requiring precipitation of MDDT-antibody complexes. Procedures for evaluating antibody specificity, titer, and avidity, and guidelines for antibody quality and usage in various applications, are generally available (Catty, *supra*; Coligan et al., *supra*).

In another embodiment of the invention, polynucleotides encoding MDDT, or any fragment or complement thereof, may be used for therapeutic purposes. In one aspect, modifications of gene expression can be achieved by designing complementary sequences or antisense molecules (DNA, RNA, PNA, or modified oligonucleotides) to the coding or regulatory regions of the gene encoding MDDT. Such technology is well known in the art, and antisense oligonucleotides or larger fragments can be designed from various locations along the coding or control regions of sequences encoding MDDT (Agrawal, S., ed. (1996) Antisense Therapeutics, Humana Press, Totawa NJ).

In therapeutic use, any gene delivery system suitable for introduction of the antisense sequences into appropriate target cells can be used. Antisense sequences can be delivered intracellularly in the form of an expression plasmid which, upon transcription, produces a sequence complementary to at least a portion of the cellular sequence encoding the target protein (Slater, J.E. et al. (1998) *J. Allergy Clin. Immunol.* 102:469-475; Scanlon, K.J. et al. (1995) 9:1288-1296). Antisense sequences can also be introduced intracellularly through the use of viral vectors, such as retrovirus and adeno-associated virus vectors (Miller, A.D. (1990) *Blood* 76:271; Ausubel et al., *supra*; Uckert, W. and W. Walther (1994) *Pharmacol. Ther.* 63:323-347). Other gene delivery mechanisms include liposome-derived systems, artificial viral envelopes, and other systems known in the art (Rossi, J.J. (1995) *Br. Med. Bull.* 51:217-225; Boado, R.J. et al. (1998) *J. Pharm. Sci.* 87:1308-1315; Morris, M.C. et al. (1997) *Nucleic Acids Res.* 25:2730-2736).

In another embodiment of the invention, polynucleotides encoding MDDT may be used for somatic or germline gene therapy. Gene therapy may be performed to (i) correct a genetic deficiency (e.g., in the cases of severe combined immunodeficiency (SCID)-X1 disease characterized by X-linked inheritance (Cavazzana-Calvo, M. et al. (2000) *Science* 288:669-672), severe combined immunodeficiency syndrome associated with an inherited adenosine deaminase (ADA) deficiency (Blaese, R.M. et al. (1995) *Science* 270:475-480; Bordignon, C. et al. (1995) *Science* 270:470-475), cystic fibrosis (Zabner, J. et al. (1993) *Cell* 75:207-216; Crystal, R.G. et al. (1995) *Hum. Gene Therapy* 6:643-666; Crystal, R.G. et al. (1995) *Hum. Gene Therapy* 6:667-703), thalassemias, familial

hypercholesterolemia, and hemophilia resulting from Factor VIII or Factor IX deficiencies (Crystal, R.G. (1995) *Science* 270:404-410; Verma, I.M. and N. Somia (1997) *Nature* 389:239-242)), (ii) express a conditionally lethal gene product (e.g., in the case of cancers which result from unregulated cell proliferation), or (iii) express a protein which affords protection against intracellular parasites (e.g., against human retroviruses, such as human immunodeficiency virus (HIV) (Baltimore, D. (1988) *Nature* 335:395-396; Poeschla, E. et al. (1996) *Proc. Natl. Acad. Sci. USA* 93:11395-11399), hepatitis B or C virus (HBV, HCV); fungal parasites, such as *Candida albicans* and *Paracoccidioides brasiliensis*; and protozoan parasites such as *Plasmodium falciparum* and *Trypanosoma cruzi*). In the case where a genetic deficiency in MDDT expression or regulation causes disease, the expression of MDDT from an appropriate population of transduced cells may alleviate the clinical manifestations caused by the genetic deficiency.

In a further embodiment of the invention, diseases or disorders caused by deficiencies in MDDT are treated by constructing mammalian expression vectors encoding MDDT and introducing these vectors by mechanical means into MDDT-deficient cells. Mechanical transfer technologies for use with cells *in vivo* or *ex vitro* include (i) direct DNA microinjection into individual cells, (ii) ballistic gold particle delivery, (iii) liposome-mediated transfection, (iv) receptor-mediated gene transfer, and (v) the use of DNA transposons (Morgan, R.A. and W.F. Anderson (1993) *Annu. Rev. Biochem.* 62:191-217; Ivics, Z. (1997) *Cell* 91:501-510; Boulay, J.-L. and H. Récipon (1998) *Curr. Opin. Biotechnol.* 9:445-450).

Expression vectors that may be effective for the expression of MDDT include, but are not limited to, the pCDNA 3.1, EPITAG, PRCCMV2, PREP, PVAX, PCR2-TOPOTA vectors (Invitrogen, Carlsbad CA), PCMV-SCRIPT, PCMV-TAG, PEGSH/PERV (Stratagene, La Jolla CA), and PTET-OFF, PTET-ON, PTRE2, PTRE2-LUC, PTK-HYG (Clontech, Palo Alto CA). MDDT may be expressed using (i) a constitutively active promoter, (e.g., from cytomegalovirus (CMV), Rous sarcoma virus (RSV), SV40 virus, thymidine kinase (TK), or  $\beta$ -actin genes), (ii) an inducible promoter (e.g., the tetracycline-regulated promoter (Gossen, M. and H. Bujard (1992) *Proc. Natl. Acad. Sci. USA* 89:5547-5551; Gossen, M. et al. (1995) *Science* 268:1766-1769; Rossi, F.M.V. and H.M. Blau (1998) *Curr. Opin. Biotechnol.* 9:451-456), commercially available in the T-REX plasmid (Invitrogen)); the ecdysone-inducible promoter (available in the plasmids PVGRXR and PIND; Invitrogen); the FK506/rapamycin inducible promoter; or the RU486/mifepristone inducible promoter (Rossi, F.M.V. and H.M. Blau, *supra*), or (iii) a tissue-specific promoter or the native promoter of the endogenous gene encoding MDDT from a normal individual.

Commercially available liposome transformation kits (e.g., the PERFECT LIPID TRANSFECTION KIT, available from Invitrogen) allow one with ordinary skill in the art to deliver polynucleotides to target cells in culture and require minimal effort to optimize experimental

parameters. In the alternative, transformation is performed using the calcium phosphate method (Graham, F.L. and A.J. Eb (1973) *Virology* 52:456-467), or by electroporation (Neumann, E. et al. (1982) *EMBO J.* 1:841-845). The introduction of DNA to primary cells requires modification of these standardized mammalian transfection protocols.

5 In another embodiment of the invention, diseases or disorders caused by genetic defects with respect to MDDT expression are treated by constructing a retrovirus vector consisting of (i) the polynucleotide encoding MDDT under the control of an independent promoter or the retrovirus long terminal repeat (LTR) promoter, (ii) appropriate RNA packaging signals, and (iii) a Rev-responsive element (RRE) along with additional retrovirus *cis*-acting RNA sequences and coding sequences  
10 required for efficient vector propagation. Retrovirus vectors (e.g., PFB and PFBNEO) are commercially available (Stratagene) and are based on published data (Riviere, I. et al. (1995) *Proc. Natl. Acad. Sci. USA* 92:6733-6737), incorporated by reference herein. The vector is propagated in an appropriate vector producing cell line (VPCL) that expresses an envelope gene with a tropism for receptors on the target cells or a promiscuous envelope protein such as VSVg (Armentano, D. et al.  
15 (1987) *J. Virol.* 61:1647-1650; Bender, M.A. et al. (1987) *J. Virol.* 61:1639-1646; Adam, M.A. and A.D. Miller (1988) *J. Virol.* 62:3802-3806; Dull, T. et al. (1998) *J. Virol.* 72:8463-8471; Zufferey, R. et al. (1998) *J. Virol.* 72:9873-9880). U.S. Patent No. 5,910,434 to Rigg ("Method for obtaining retrovirus packaging cell lines producing high transducing efficiency retroviral supernatant") discloses a method for obtaining retrovirus packaging cell lines and is hereby incorporated by  
20 reference. Propagation of retrovirus vectors, transduction of a population of cells (e.g., CD4<sup>+</sup> T-cells), and the return of transduced cells to a patient are procedures well known to persons skilled in the art of gene therapy and have been well documented (Ranga, U. et al. (1997) *J. Virol.* 71:7020-7029; Bauer, G. et al. (1997) *Blood* 89:2259-2267; Bonyhadi, M.L. (1997) *J. Virol.* 71:4707-4716; Ranga, U. et al. (1998) *Proc. Natl. Acad. Sci. USA* 95:1201-1206; Su, L. (1997) *Blood* 89:2283-  
25 2290).

In an embodiment, an adenovirus-based gene therapy delivery system is used to deliver polynucleotides encoding MDDT to cells which have one or more genetic abnormalities with respect to the expression of MDDT. The construction and packaging of adenovirus-based vectors are well known to those with ordinary skill in the art. Replication defective adenovirus vectors have proven to  
30 be versatile for importing genes encoding immunoregulatory proteins into intact islets in the pancreas (Csete, M.E. et al. (1995) *Transplantation* 27:263-268). Potentially useful adenoviral vectors are described in U.S. Patent No. 5,707,618 to Armentano ("Adenovirus vectors for gene therapy"), hereby incorporated by reference. For adenoviral vectors, see also Antinozzi, P.A. et al. (1999; *Annu. Rev. Nutr.* 19:511-544) and Verma, I.M. and N. Somia (1997; *Nature* 18:389:239-242).

35 In another embodiment, a herpes-based, gene therapy delivery system is used to deliver

polynucleotides encoding MDDT to target cells which have one or more genetic abnormalities with respect to the expression of MDDT. The use of herpes simplex virus (HSV)-based vectors may be especially valuable for introducing MDDT to cells of the central nervous system, for which HSV has a tropism. The construction and packaging of herpes-based vectors are well known to those with  
5 ordinary skill in the art. A replication-competent herpes simplex virus (HSV) type 1-based vector has been used to deliver a reporter gene to the eyes of primates (Liu, X. et al. (1999) *Exp. Eye Res.* 169:385-395). The construction of a HSV-1 virus vector has also been disclosed in detail in U.S. Patent No. 5,804,413 to DeLuca ("Herpes simplex virus strains for gene transfer"), which is hereby incorporated by reference. U.S. Patent No. 5,804,413 teaches the use of recombinant HSV d92 which  
10 consists of a genome containing at least one exogenous gene to be transferred to a cell under the control of the appropriate promoter for purposes including human gene therapy. Also taught by this patent are the construction and use of recombinant HSV strains deleted for ICP4, ICP27 and ICP22. For HSV vectors, see also Goins, W.F. et al. (1999; *J. Virol.* 73:519-532) and Xu, H. et al. (1994; *Dev. Biol.* 163:152-161). The manipulation of cloned herpesvirus sequences, the generation of  
15 recombinant virus following the transfection of multiple plasmids containing different segments of the large herpesvirus genomes, the growth and propagation of herpesvirus, and the infection of cells with herpesvirus are techniques well known to those of ordinary skill in the art.

In another embodiment, an alphavirus (positive, single-stranded RNA virus) vector is used to deliver polynucleotides encoding MDDT to target cells. The biology of the prototypic alphavirus,  
20 Semliki Forest Virus (SFV), has been studied extensively and gene transfer vectors have been based on the SFV genome (Garoff, H. and K.-J. Li (1998) *Curr. Opin. Biotechnol.* 9:464-469). During alphavirus RNA replication, a subgenomic RNA is generated that normally encodes the viral capsid proteins. This subgenomic RNA replicates to higher levels than the full length genomic RNA, resulting in the overproduction of capsid proteins relative to the viral proteins with enzymatic activity  
25 (e.g., protease and polymerase). Similarly, inserting the coding sequence for MDDT into the alphavirus genome in place of the capsid-coding region results in the production of a large number of MDDT-coding RNAs and the synthesis of high levels of MDDT in vector transduced cells. While alphavirus infection is typically associated with cell lysis within a few days, the ability to establish a persistent infection in hamster normal kidney cells (BHK-21) with a variant of Sindbis virus (SIN)  
30 indicates that the lytic replication of alphaviruses can be altered to suit the needs of the gene therapy application (Dryga, S.A. et al. (1997) *Virology* 228:74-83). The wide host range of alphaviruses will allow the introduction of MDDT into a variety of cell types. The specific transduction of a subset of cells in a population may require the sorting of cells prior to transduction. The methods of manipulating infectious cDNA clones of alphaviruses, performing alphavirus cDNA and RNA  
35 transfections, and performing alphavirus infections, are well known to those with ordinary skill in the

art.

Oligonucleotides derived from the transcription initiation site, e.g., between about positions -10 and +10 from the start site, may also be employed to inhibit gene expression. Similarly, inhibition can be achieved using triple helix base-pairing methodology. Triple helix pairing is useful because it causes inhibition of the ability of the double helix to open sufficiently for the binding of polymerases, transcription factors, or regulatory molecules. Recent therapeutic advances using triplex DNA have been described in the literature (Gee, J.E. et al. (1994) in Huber, B.E. and B.I. Carr, Molecular and Immunologic Approaches, Futura Publishing, Mt. Kisco NY, pp. 163-177). A complementary sequence or antisense molecule may also be designed to block translation of mRNA by preventing the transcript from binding to ribosomes.

Ribozymes, enzymatic RNA molecules, may also be used to catalyze the specific cleavage of RNA. The mechanism of ribozyme action involves sequence-specific hybridization of the ribozyme molecule to complementary target RNA, followed by endonucleolytic cleavage. For example, engineered hammerhead motif ribozyme molecules may specifically and efficiently catalyze endonucleolytic cleavage of RNA molecules encoding MDDT.

Specific ribozyme cleavage sites within any potential RNA target are initially identified by scanning the target molecule for ribozyme cleavage sites, including the following sequences: GUA, GUU, and GUC. Once identified, short RNA sequences of between 15 and 20 ribonucleotides, corresponding to the region of the target gene containing the cleavage site, may be evaluated for secondary structural features which may render the oligonucleotide inoperable. The suitability of candidate targets may also be evaluated by testing accessibility to hybridization with complementary oligonucleotides using ribonuclease protection assays.

Complementary ribonucleic acid molecules and ribozymes may be prepared by any method known in the art for the synthesis of nucleic acid molecules. These include techniques for chemically synthesizing oligonucleotides such as solid phase phosphoramidite chemical synthesis. Alternatively, RNA molecules may be generated by *in vitro* and *in vivo* transcription of DNA molecules encoding MDDT. Such DNA sequences may be incorporated into a wide variety of vectors with suitable RNA polymerase promoters such as T7 or SP6. Alternatively, these cDNA constructs that synthesize complementary RNA, constitutively or inducibly, can be introduced into cell lines, cells, or tissues.

RNA molecules may be modified to increase intracellular stability and half-life. Possible modifications include, but are not limited to, the addition of flanking sequences at the 5' and/or 3' ends of the molecule, or the use of phosphorothioate or 2' O-methyl rather than phosphodiesterase linkages within the backbone of the molecule. This concept is inherent in the production of PNAs and can be extended in all of these molecules by the inclusion of nontraditional bases such as inosine, queosine, and wybutosine, as well as acetyl-, methyl-, thio-, and similarly modified forms of adenine,

cytidine, guanine, thymine, and uridine which are not as easily recognized by endogenous endonucleases.

An additional embodiment of the invention encompasses a method for screening for a compound which is effective in altering expression of a polynucleotide encoding MDDT.

5 Compounds which may be effective in altering expression of a specific polynucleotide may include, but are not limited to, oligonucleotides, antisense oligonucleotides, triple helix-forming oligonucleotides, transcription factors and other polypeptide transcriptional regulators, and non-macromolecular chemical entities which are capable of interacting with specific polynucleotide sequences. Effective compounds may alter polynucleotide expression by acting as either inhibitors or  
10 promoters of polynucleotide expression. Thus, in the treatment of disorders associated with increased MDDT expression or activity, a compound which specifically inhibits expression of the polynucleotide encoding MDDT may be therapeutically useful, and in the treatment of disorders associated with decreased MDDT expression or activity, a compound which specifically promotes expression of the polynucleotide encoding MDDT may be therapeutically useful.

15 At least one, and up to a plurality, of test compounds may be screened for effectiveness in altering expression of a specific polynucleotide. A test compound may be obtained by any method commonly known in the art, including chemical modification of a compound known to be effective in altering polynucleotide expression; selection from an existing, commercially-available or proprietary library of naturally-occurring or non-natural chemical compounds; rational design of a compound  
20 based on chemical and/or structural properties of the target polynucleotide; and selection from a library of chemical compounds created combinatorially or randomly. A sample comprising a polynucleotide encoding MDDT is exposed to at least one test compound thus obtained. The sample may comprise, for example, an intact or permeabilized cell, or an *in vitro* cell-free or reconstituted biochemical system. Alterations in the expression of a polynucleotide encoding MDDT are assayed  
25 by any method commonly known in the art. Typically, the expression of a specific nucleotide is detected by hybridization with a probe having a nucleotide sequence complementary to the sequence of the polynucleotide encoding MDDT. The amount of hybridization may be quantified, thus forming the basis for a comparison of the expression of the polynucleotide both with and without exposure to one or more test compounds. Detection of a change in the expression of a polynucleotide  
30 exposed to a test compound indicates that the test compound is effective in altering the expression of the polynucleotide. A screen for a compound effective in altering expression of a specific polynucleotide can be carried out, for example, using a *Schizosaccharomyces pombe* gene expression system (Atkins, D. et al. (1999) U.S. Patent No. 5,932,435; Arndt, G.M. et al. (2000) Nucleic Acids Res. 28:E15) or a human cell line such as HeLa cell (Clarke, M.L. et al. (2000) Biochem. Biophys. Res. Commun. 268:8-13). A particular embodiment of the present invention involves screening a  
35



combinatorial library of oligonucleotides (such as deoxyribonucleotides, ribonucleotides, peptide nucleic acids, and modified oligonucleotides) for antisense activity against a specific polynucleotide sequence (Bruice, T.W. et al. (1997) U.S. Patent No. 5,686,242; Bruice, T.W. et al. (2000) U.S. Patent No. 6,022,691).

5 Many methods for introducing vectors into cells or tissues are available and equally suitable for use *in vivo*, *in vitro*, and *ex vivo*. For *ex vivo* therapy, vectors may be introduced into stem cells taken from the patient and clonally propagated for autologous transplant back into that same patient. Delivery by transfection, by liposome injections, or by polycationic amino polymers may be achieved using methods which are well known in the art (Goldman, C.K. et al. (1997) Nat. Biotechnol. 15:462-  
10 466).

Any of the therapeutic methods described above may be applied to any subject in need of such therapy, including, for example, mammals such as humans, dogs, cats, cows, horses, rabbits, and monkeys.

An additional embodiment of the invention relates to the administration of a composition  
15 which generally comprises an active ingredient formulated with a pharmaceutically acceptable excipient. Excipients may include, for example, sugars, starches, celluloses, gums, and proteins. Various formulations are commonly known and are thoroughly discussed in the latest edition of Remington's Pharmaceutical Sciences (Maack Publishing, Easton PA). Such compositions may consist of MDDT, antibodies to MDDT, and mimetics, agonists, antagonists, or inhibitors of MDDT.

20 The compositions utilized in this invention may be administered by any number of routes including, but not limited to, oral, intravenous, intramuscular, intra-arterial, intramedullary, intrathecal, intraventricular, pulmonary, transdermal, subcutaneous, intraperitoneal, intranasal, enteral, topical, sublingual, or rectal means.

Compositions for pulmonary administration may be prepared in liquid or dry powder form.  
25 These compositions are generally aerosolized immediately prior to inhalation by the patient. In the case of small molecules (e.g. traditional low molecular weight organic drugs), aerosol delivery of fast-acting formulations is well-known in the art. In the case of macromolecules (e.g. larger peptides and proteins), recent developments in the field of pulmonary delivery via the alveolar region of the lung have enabled the practical delivery of drugs such as insulin to blood circulation (see, e.g., Patton,  
30 J.S. et al., U.S. Patent No. 5,997,848). Pulmonary delivery has the advantage of administration without needle injection, and obviates the need for potentially toxic penetration enhancers.

Compositions suitable for use in the invention include compositions wherein the active ingredients are contained in an effective amount to achieve the intended purpose. The determination of an effective dose is well within the capability of those skilled in the art.

35 Specialized forms of compositions may be prepared for direct intracellular delivery of

macromolecules comprising MDDT or fragments thereof. For example, liposome preparations containing a cell-impermeable macromolecule may promote cell fusion and intracellular delivery of the macromolecule. Alternatively, MDDT or a fragment thereof may be joined to a short cationic N-terminal portion from the HIV Tat-1 protein. Fusion proteins thus generated have been found to  
5 transduce into the cells of all tissues, including the brain, in a mouse model system (Schwarze, S.R. et al. (1999) Science 285:1569-1572).

For any compound, the therapeutically effective dose can be estimated initially either in cell culture assays, e.g., of neoplastic cells, or in animal models such as mice, rats, rabbits, dogs, monkeys, or pigs. An animal model may also be used to determine the appropriate concentration  
10 range and route of administration. Such information can then be used to determine useful doses and routes for administration in humans.

A therapeutically effective dose refers to that amount of active ingredient, for example MDDT or fragments thereof, antibodies of MDDT, and agonists, antagonists or inhibitors of MDDT, which ameliorates the symptoms or condition. Therapeutic efficacy and toxicity may be determined  
15 by standard pharmaceutical procedures in cell cultures or with experimental animals, such as by calculating the  $ED_{50}$  (the dose therapeutically effective in 50% of the population) or  $LD_{50}$  (the dose lethal to 50% of the population) statistics. The dose ratio of toxic to therapeutic effects is the therapeutic index, which can be expressed as the  $LD_{50}/ED_{50}$  ratio. Compositions which exhibit large therapeutic indices are preferred. The data obtained from cell culture assays and animal studies are  
20 used to formulate a range of dosage for human use. The dosage contained in such compositions is preferably within a range of circulating concentrations that includes the  $ED_{50}$  with little or no toxicity. The dosage varies within this range depending upon the dosage form employed, the sensitivity of the patient, and the route of administration.

The exact dosage will be determined by the practitioner, in light of factors related to the  
25 subject requiring treatment. Dosage and administration are adjusted to provide sufficient levels of the active moiety or to maintain the desired effect. Factors which may be taken into account include the severity of the disease state, the general health of the subject, the age, weight, and gender of the subject, time and frequency of administration, drug combination(s), reaction sensitivities, and response to therapy. Long-acting compositions may be administered every 3 to 4 days, every week,  
30 or biweekly depending on the half-life and clearance rate of the particular formulation.

Normal dosage amounts may vary from about 0.1  $\mu\text{g}$  to 100,000  $\mu\text{g}$ , up to a total dose of about 1 gram, depending upon the route of administration. Guidance as to particular dosages and methods of delivery is provided in the literature and generally available to practitioners in the art. Those skilled in the art will employ different formulations for nucleotides than for proteins or their  
35 inhibitors. Similarly, delivery of polynucleotides or polypeptides will be specific to particular cells,

conditions, locations, etc.

## DIAGNOSTICS

In another embodiment, antibodies which specifically bind MDDT may be used for the diagnosis of disorders characterized by expression of MDDT, or in assays to monitor patients being  
5 treated with MDDT or agonists, antagonists, or inhibitors of MDDT. Antibodies useful for diagnostic purposes may be prepared in the same manner as described above for therapeutics. Diagnostic assays for MDDT include methods which utilize the antibody and a label to detect MDDT in human body fluids or in extracts of cells or tissues. The antibodies may be used with or without modification, and may be labeled by covalent or non-covalent attachment of a reporter molecule. A wide variety of  
10 reporter molecules, several of which are described above, are known in the art and may be used.

A variety of protocols for measuring MDDT, including ELISAs, RIAs, and FACS, are known in the art and provide a basis for diagnosing altered or abnormal levels of MDDT expression. Normal or standard values for MDDT expression are established by combining body fluids or cell extracts taken from normal mammalian subjects, for example, human subjects, with antibodies to MDDT  
15 under conditions suitable for complex formation. The amount of standard complex formation may be quantitated by various methods, such as photometric means. Quantities of MDDT expressed in subject, control, and disease samples from biopsied tissues are compared with the standard values. Deviation between standard and subject values establishes the parameters for diagnosing disease.

In another embodiment of the invention, polynucleotides encoding MDDT may be used for  
20 diagnostic purposes. The polynucleotides which may be used include oligonucleotides, complementary RNA and DNA molecules, and PNAs. The polynucleotides may be used to detect and quantify gene expression in biopsied tissues in which expression of MDDT may be correlated with disease. The diagnostic assay may be used to determine absence, presence, and excess expression of MDDT, and to monitor regulation of MDDT levels during therapeutic intervention.

In one aspect, hybridization with PCR probes which are capable of detecting polynucleotides, including genomic sequences, encoding MDDT or closely related molecules may be used to identify  
25 nucleic acid sequences which encode MDDT. The specificity of the probe, whether it is made from a highly specific region, e.g., the 5' regulatory region, or from a less specific region, e.g., a conserved motif, and the stringency of the hybridization or amplification will determine whether the probe  
30 identifies only naturally occurring sequences encoding MDDT, allelic variants, or related sequences.

Probes may also be used for the detection of related sequences, and may have at least 50% sequence identity to any of the MDDT encoding sequences. The hybridization probes of the subject invention may be DNA or RNA and may be derived from the sequence of SEQ ID NO:57-112 or from genomic sequences including promoters, enhancers, and introns of the MDDT gene.

35 Means for producing specific hybridization probes for polynucleotides encoding MDDT

include the cloning of polynucleotides encoding MDDT or MDDT derivatives into vectors for the production of mRNA probes. Such vectors are known in the art, are commercially available, and may be used to synthesize RNA probes *in vitro* by means of the addition of the appropriate RNA polymerases and the appropriate labeled nucleotides. Hybridization probes may be labeled by a  
5 variety of reporter groups, for example, by radionuclides such as <sup>32</sup>P or <sup>35</sup>S, or by enzymatic labels, such as alkaline phosphatase coupled to the probe via avidin/biotin coupling systems, and the like.

Polynucleotides encoding MDDT may be used for the diagnosis of disorders associated with expression of MDDT. Examples of such disorders include, but are not limited to, a cell proliferative disorder such as actinic keratosis, arteriosclerosis, atherosclerosis, bursitis, cirrhosis, hepatitis, mixed  
10 connective tissue disease (MCTD), myelofibrosis, paroxysmal nocturnal hemoglobinuria, polycythemia vera, psoriasis, primary thrombocythemia, and cancers including adenocarcinoma, leukemia, lymphoma, melanoma, myeloma, sarcoma, teratocarcinoma, and, in particular, cancers of the adrenal gland, bladder, bone, bone marrow, brain, breast, cervix, gall bladder, ganglia, gastrointestinal tract, heart, kidney, liver, lung, muscle, ovary, pancreas, parathyroid, penis, prostate,  
15 salivary glands, skin, spleen, testis, thymus, thyroid, and uterus; an autoimmune/inflammatory disorder such as acquired immunodeficiency syndrome (AIDS), Addison's disease, adult respiratory distress syndrome, allergies, ankylosing spondylitis, amyloidosis, anemia, asthma, atherosclerosis, autoimmune hemolytic anemia, autoimmune thyroiditis, autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy (APECED), bronchitis, cholecystitis, contact dermatitis, Crohn's  
20 disease, atopic dermatitis, dermatomyositis, diabetes mellitus, emphysema, episodic lymphopenia with lymphocytotoxins, erythroblastosis fetalis, erythema nodosum, atrophic gastritis, glomerulonephritis, Goodpasture's syndrome, gout, Graves' disease, Hashimoto's thyroiditis, hypereosinophilia, irritable bowel syndrome, multiple sclerosis, myasthenia gravis, myocardial or pericardial inflammation, osteoarthritis, osteoporosis, pancreatitis, polymyositis, psoriasis, Reiter's  
25 syndrome, rheumatoid arthritis, scleroderma, Sjögren's syndrome, systemic anaphylaxis, systemic lupus erythematosus, systemic sclerosis, thrombocytopenic purpura, ulcerative colitis, uveitis, Werner syndrome, complications of cancer, hemodialysis, and extracorporeal circulation, viral, bacterial, fungal, parasitic, protozoal, and helminthic infections, and trauma; a disease treated with a steroid and a disorder caused by the metabolic response to treatment with steroids, such as  
30 adenomatosis, cholestasis, cirrhosis, hemangioma, Henoch-Schonlein purpura, hepatitis, hepatocellular and metastatic carcinomas, idiopathic thrombocytopenic purpura, porphyria, sarcoidosis, and Wilson disease; a developmental disorder such as renal tubular acidosis, anemia, Cushing's syndrome, achondroplastic dwarfism, Duchenne and Becker muscular dystrophy, epilepsy, gonadal dysgenesis, WAGR syndrome (Wilms' tumor, aniridia, genitourinary abnormalities, and  
35 mental retardation), Smith-Magenis syndrome, myelodysplastic syndrome, hereditary mucoepithelial

dysplasia, hereditary keratodermas, hereditary neuropathies such as Charcot-Marie-Tooth disease and neurofibromatosis, hypothyroidism, hydrocephalus, seizure disorders such as Sydenham's chorea and cerebral palsy, spina bifida, anencephaly, craniorachischisis, congenital glaucoma, cataract, and sensorineural hearing loss; and a neurological disorder such as epilepsy, ischemic cerebrovascular disease, stroke, cerebral neoplasms, Alzheimer's disease, Pick's disease, Huntington's disease, dementia, Parkinson's disease and other extrapyramidal disorders, amyotrophic lateral sclerosis and other motor neuron disorders, progressive neural muscular atrophy, retinitis pigmentosa, hereditary ataxias, multiple sclerosis and other demyelinating diseases, bacterial and viral meningitis, brain abscess, subdural empyema, epidural abscess, suppurative intracranial thrombophlebitis, myelitis and radiculitis, viral central nervous system disease, prion diseases including kuru, Creutzfeldt-Jakob disease, and Gerstmann-Straussler-Scheinker syndrome, fatal familial insomnia, nutritional and metabolic diseases of the nervous system, neurofibromatosis, tuberous sclerosis, cerebelloretinal hemangioblastomatosis, encephalotrigeminal syndrome, mental retardation and other developmental disorders of the central nervous system including Down syndrome, cerebral palsy, neuroskeletal disorders, autonomic nervous system disorders, cranial nerve disorders, spinal cord diseases, muscular dystrophy and other neuromuscular disorders, peripheral nervous system disorders, dermatomyositis and polymyositis, inherited, metabolic, endocrine, and toxic myopathies, myasthenia gravis, periodic paralysis, mental disorders including mood, anxiety, and schizophrenic disorders, seasonal affective disorder (SAD), akathisia, amnesia, catatonia, diabetic neuropathy, tardive dyskinesia, dystonias, paranoid psychoses, postherpetic neuralgia, Tourette's disorder, progressive supranuclear palsy, corticobasal degeneration, and familial frontotemporal dementia . SEQ ID NO:58, encoding SEQ ID NO:2, and SEQ ID NO:2 can be used in the diagnosis and treatment of Tangier disease and SEQ ID NO:61, encoding SEQ ID NO:5, and SEQ ID NO:5 can be used in the diagnosis and treatment of type II diabetes. Polynucleotides encoding MDDT may be used in Southern or northern analysis, dot blot, or other membrane-based technologies; in PCR technologies; in dipstick, pin, and multiformat ELISA-like assays; and in microarrays utilizing fluids or tissues from patients to detect altered MDDT expression. Such qualitative or quantitative methods are well known in the art.

In a particular aspect, polynucleotides encoding MDDT may be used in assays that detect the presence of associated disorders, particularly those mentioned above. Polynucleotides complementary to sequences encoding MDDT may be labeled by standard methods and added to a fluid or tissue sample from a patient under conditions suitable for the formation of hybridization complexes. After a suitable incubation period, the sample is washed and the signal is quantified and compared with a standard value. If the amount of signal in the patient sample is significantly altered in comparison to a control sample then the presence of altered levels of polynucleotides encoding

MDDT in the sample indicates the presence of the associated disorder. Such assays may also be used to evaluate the efficacy of a particular therapeutic treatment regimen in animal studies, in clinical trials, or to monitor the treatment of an individual patient.

In order to provide a basis for the diagnosis of a disorder associated with expression of MDDT, a normal or standard profile for expression is established. This may be accomplished by combining body fluids or cell extracts taken from normal subjects, either animal or human, with a sequence, or a fragment thereof, encoding MDDT, under conditions suitable for hybridization or amplification. Standard hybridization may be quantified by comparing the values obtained from normal subjects with values from an experiment in which a known amount of a substantially purified polynucleotide is used. Standard values obtained in this manner may be compared with values obtained from samples from patients who are symptomatic for a disorder. Deviation from standard values is used to establish the presence of a disorder.

Once the presence of a disorder is established and a treatment protocol is initiated, hybridization assays may be repeated on a regular basis to determine if the level of expression in the patient begins to approximate that which is observed in the normal subject. The results obtained from successive assays may be used to show the efficacy of treatment over a period ranging from several days to months.

With respect to cancer, the presence of an abnormal amount of transcript (either under- or overexpressed) in biopsied tissue from an individual may indicate a predisposition for the development of the disease, or may provide a means for detecting the disease prior to the appearance of actual clinical symptoms. A more definitive diagnosis of this type may allow health professionals to employ preventative measures or aggressive treatment earlier, thereby preventing the development or further progression of the cancer.

Additional diagnostic uses for oligonucleotides designed from the sequences encoding MDDT may involve the use of PCR. These oligomers may be chemically synthesized, generated enzymatically, or produced *in vitro*. Oligomers will preferably contain a fragment of a polynucleotide encoding MDDT, or a fragment of a polynucleotide complementary to the polynucleotide encoding MDDT, and will be employed under optimized conditions for identification of a specific gene or condition. Oligomers may also be employed under less stringent conditions for detection or quantification of closely related DNA or RNA sequences.

In a particular aspect, oligonucleotide primers derived from polynucleotides encoding MDDT may be used to detect single nucleotide polymorphisms (SNPs). SNPs are substitutions, insertions and deletions that are a frequent cause of inherited or acquired genetic disease in humans. Methods of SNP detection include, but are not limited to, single-stranded conformation polymorphism (SSCP) and fluorescent SSCP (fSSCP) methods. In SSCP, oligonucleotide primers derived from

polynucleotides encoding MDDT are used to amplify DNA using the polymerase chain reaction (PCR). The DNA may be derived, for example, from diseased or normal tissue, biopsy samples, bodily fluids, and the like. SNPs in the DNA cause differences in the secondary and tertiary structures of PCR products in single-stranded form, and these differences are detectable using gel electrophoresis in non-denaturing gels. In fSCCP, the oligonucleotide primers are fluorescently labeled, which allows detection of the amplimers in high-throughput equipment such as DNA sequencing machines. Additionally, sequence database analysis methods, termed *in silico* SNP (isSNP), are capable of identifying polymorphisms by comparing the sequence of individual overlapping DNA fragments which assemble into a common consensus sequence. These computer-based methods filter out sequence variations due to laboratory preparation of DNA and sequencing errors using statistical models and automated analyses of DNA sequence chromatograms. In the alternative, SNPs may be detected and characterized by mass spectrometry using, for example, the high throughput MASSARRAY system (Sequenom, Inc., San Diego CA).

SNPs may be used to study the genetic basis of human disease. For example, at least 16 common SNPs have been associated with non-insulin-dependent diabetes mellitus. SNPs are also useful for examining differences in disease outcomes in monogenic disorders, such as cystic fibrosis, sickle cell anemia, or chronic granulomatous disease. For example, variants in the mannose-binding lectin, MBL2, have been shown to be correlated with deleterious pulmonary outcomes in cystic fibrosis. SNPs also have utility in pharmacogenomics, the identification of genetic variants that influence a patient's response to a drug, such as life-threatening toxicity. For example, a variation in N-acetyl transferase is associated with a high incidence of peripheral neuropathy in response to the anti-tuberculosis drug isoniazid, while a variation in the core promoter of the ALOX5 gene results in diminished clinical response to treatment with an anti-asthma drug that targets the 5-lipoxygenase pathway. Analysis of the distribution of SNPs in different populations is useful for investigating genetic drift, mutation, recombination, and selection, as well as for tracing the origins of populations and their migrations (Taylor, J.G. et al. (2001) *Trends Mol. Med.* 7:507-512; Kwok, P.-Y. and Z. Gu (1999) *Mol. Med. Today* 5:538-543; Nowotny, P. et al. (2001) *Curr. Opin. Neurobiol.* 11:637-641).

Methods which may also be used to quantify the expression of MDDT include radiolabeling or biotinylating nucleotides, coamplification of a control nucleic acid, and interpolating results from standard curves (Melby, P.C. et al. (1993) *J. Immunol. Methods* 159:235-244; Duplaa, C. et al. (1993) *Anal. Biochem.* 212:229-236). The speed of quantitation of multiple samples may be accelerated by running the assay in a high-throughput format where the oligomer or polynucleotide of interest is presented in various dilutions and a spectrophotometric or colorimetric response gives rapid quantitation.

In further embodiments, oligonucleotides or longer fragments derived from any of the

polynucleotides described herein may be used as elements on a microarray. The microarray can be used in transcript imaging techniques which monitor the relative expression levels of large numbers of genes simultaneously as described below. The microarray may also be used to identify genetic variants, mutations, and polymorphisms. This information may be used to determine gene function, to understand the genetic basis of a disorder, to diagnose a disorder, to monitor progression/regression of disease as a function of gene expression, and to develop and monitor the activities of therapeutic agents in the treatment of disease. In particular, this information may be used to develop a pharmacogenomic profile of a patient in order to select the most appropriate and effective treatment regimen for that patient. For example, therapeutic agents which are highly effective and display the fewest side effects may be selected for a patient based on his/her pharmacogenomic profile.

In another embodiment, MDDT, fragments of MDDT, or antibodies specific for MDDT may be used as elements on a microarray. The microarray may be used to monitor or measure protein-protein interactions, drug-target interactions, and gene expression profiles, as described above.

A particular embodiment relates to the use of the polynucleotides of the present invention to generate a transcript image of a tissue or cell type. A transcript image represents the global pattern of gene expression by a particular tissue or cell type. Global gene expression patterns are analyzed by quantifying the number of expressed genes and their relative abundance under given conditions and at a given time (Seilhamer et al., "Comparative Gene Transcript Analysis," U.S. Patent No. 5,840,484; hereby expressly incorporated by reference herein). Thus a transcript image may be generated by hybridizing the polynucleotides of the present invention or their complements to the totality of transcripts or reverse transcripts of a particular tissue or cell type. In one embodiment, the hybridization takes place in high-throughput format, wherein the polynucleotides of the present invention or their complements comprise a subset of a plurality of elements on a microarray. The resultant transcript image would provide a profile of gene activity.

Transcript images may be generated using transcripts isolated from tissues, cell lines, biopsies, or other biological samples. The transcript image may thus reflect gene expression *in vivo*, as in the case of a tissue or biopsy sample, or *in vitro*, as in the case of a cell line.

Transcript images which profile the expression of the polynucleotides of the present invention may also be used in conjunction with *in vitro* model systems and preclinical evaluation of pharmaceuticals, as well as toxicological testing of industrial and naturally-occurring environmental compounds. All compounds induce characteristic gene expression patterns, frequently termed molecular fingerprints or toxicant signatures, which are indicative of mechanisms of action and toxicity (Nuwaysir, E.F. et al. (1999) Mol. Carcinog. 24:153-159; Steiner, S. and N.L. Anderson (2000) Toxicol. Lett. 112-113:467-471). If a test compound has a signature similar to that of a



compound with known toxicity, it is likely to share those toxic properties. These fingerprints or signatures are most useful and refined when they contain expression information from a large number of genes and gene families. Ideally, a genome-wide measurement of expression provides the highest quality signature. Even genes whose expression is not altered by any tested compounds are important as well, as the levels of expression of these genes are used to normalize the rest of the expression data. The normalization procedure is useful for comparison of expression data after treatment with different compounds. While the assignment of gene function to elements of a toxicant signature aids in interpretation of toxicity mechanisms, knowledge of gene function is not necessary for the statistical matching of signatures which leads to prediction of toxicity (see, for example, Press Release 00-02 from the National Institute of Environmental Health Sciences, released February 29, 2000, available at <http://www.niehs.nih.gov/oc/news/toxchip.htm>). Therefore, it is important and desirable in toxicological screening using toxicant signatures to include all expressed gene sequences.

In an embodiment, the toxicity of a test compound can be assessed by treating a biological sample containing nucleic acids with the test compound. Nucleic acids that are expressed in the treated biological sample are hybridized with one or more probes specific to the polynucleotides of the present invention, so that transcript levels corresponding to the polynucleotides of the present invention may be quantified. The transcript levels in the treated biological sample are compared with levels in an untreated biological sample. Differences in the transcript levels between the two samples are indicative of a toxic response caused by the test compound in the treated sample.

Another embodiment relates to the use of the polypeptides disclosed herein to analyze the proteome of a tissue or cell type. The term proteome refers to the global pattern of protein expression in a particular tissue or cell type. Each protein component of a proteome can be subjected individually to further analysis. Proteome expression patterns, or profiles, are analyzed by quantifying the number of expressed proteins and their relative abundance under given conditions and at a given time. A profile of a cell's proteome may thus be generated by separating and analyzing the polypeptides of a particular tissue or cell type. In one embodiment, the separation is achieved using two-dimensional gel electrophoresis, in which proteins from a sample are separated by isoelectric focusing in the first dimension, and then according to molecular weight by sodium dodecyl sulfate slab gel electrophoresis in the second dimension (Steiner and Anderson, *supra*). The proteins are visualized in the gel as discrete and uniquely positioned spots, typically by staining the gel with an agent such as Coomassie Blue or silver or fluorescent stains. The optical density of each protein spot is generally proportional to the level of the protein in the sample. The optical densities of equivalently positioned protein spots from different samples, for example, from biological samples either treated or untreated with a test compound or therapeutic agent, are compared to identify any changes in protein spot density related to the treatment. The proteins in the spots are partially

sequenced using, for example, standard methods employing chemical or enzymatic cleavage followed by mass spectrometry. The identity of the protein in a spot may be determined by comparing its partial sequence, preferably of at least 5 contiguous amino acid residues, to the polypeptide sequences of interest. In some cases, further sequence data may be obtained for definitive protein identification.

5 A proteomic profile may also be generated using antibodies specific for MDDT to quantify the levels of MDDT expression. In one embodiment, the antibodies are used as elements on a microarray, and protein expression levels are quantified by exposing the microarray to the sample and detecting the levels of protein bound to each array element (Lueking, A. et al. (1999) *Anal. Biochem.* 270:103-111; Mendoe, L.G. et al. (1999) *Biotechniques* 27:778-788). Detection may be performed  
10 by a variety of methods known in the art, for example, by reacting the proteins in the sample with a thiol- or amino-reactive fluorescent compound and detecting the amount of fluorescence bound at each array element.

Toxicant signatures at the proteome level are also useful for toxicological screening, and should be analyzed in parallel with toxicant signatures at the transcript level. There is a poor  
15 correlation between transcript and protein abundances for some proteins in some tissues (Anderson, N.L. and J. Seilhamer (1997) *Electrophoresis* 18:533-537), so proteome toxicant signatures may be useful in the analysis of compounds which do not significantly affect the transcript image, but which alter the proteomic profile. In addition, the analysis of transcripts in body fluids is difficult, due to rapid degradation of mRNA, so proteomic profiling may be more reliable and informative in such  
20 cases.

In another embodiment, the toxicity of a test compound is assessed by treating a biological sample containing proteins with the test compound. Proteins that are expressed in the treated biological sample are separated so that the amount of each protein can be quantified. The amount of each protein is compared to the amount of the corresponding protein in an untreated biological  
25 sample. A difference in the amount of protein between the two samples is indicative of a toxic response to the test compound in the treated sample. Individual proteins are identified by sequencing the amino acid residues of the individual proteins and comparing these partial sequences to the polypeptides of the present invention.

In another embodiment, the toxicity of a test compound is assessed by treating a biological  
30 sample containing proteins with the test compound. Proteins from the biological sample are incubated with antibodies specific to the polypeptides of the present invention. The amount of protein recognized by the antibodies is quantified. The amount of protein in the treated biological sample is compared with the amount in an untreated biological sample. A difference in the amount of protein between the two samples is indicative of a toxic response to the test compound in the treated  
35 sample.

Microarrays may be prepared, used, and analyzed using methods known in the art (Brennan, T.M. et al. (1995) U.S. Patent No. 5,474,796; Schena, M. et al. (1996) Proc. Natl. Acad. Sci. USA 93:10614-10619; Baldeschweiler et al. (1995) PCT application WO95/251116; Shalon, D. et al. (1995) PCT application WO95/35505; Heller, R.A. et al. (1997) Proc. Natl. Acad. Sci. USA 94:2150-2155; Heller, M.J. et al. (1997) U.S. Patent No. 5,605,662). Various types of microarrays are well known and thoroughly described in Schena, M., ed. (1999; DNA Microarrays: A Practical Approach, Oxford University Press, London).

In another embodiment of the invention, nucleic acid sequences encoding MDDT may be used to generate hybridization probes useful in mapping the naturally occurring genomic sequence. Either coding or noncoding sequences may be used, and in some instances, noncoding sequences may be preferable over coding sequences. For example, conservation of a coding sequence among members of a multi-gene family may potentially cause undesired cross hybridization during chromosomal mapping. The sequences may be mapped to a particular chromosome, to a specific region of a chromosome, or to artificial chromosome constructions, e.g., human artificial chromosomes (HACs), yeast artificial chromosomes (YACs), bacterial artificial chromosomes (BACs), bacterial P1 constructions, or single chromosome cDNA libraries (Harrington, J.J. et al. (1997) Nat. Genet. 15:345-355; Price, C.M. (1993) Blood Rev. 7:127-134; Trask, B.J. (1991) Trends Genet. 7:149-154). Once mapped, the nucleic acid sequences may be used to develop genetic linkage maps, for example, which correlate the inheritance of a disease state with the inheritance of a particular chromosome region or restriction fragment length polymorphism (RFLP) (Lander, E.S. and D. Botstein (1986) Proc. Natl. Acad. Sci. USA 83:7353-7357).

Fluorescent *in situ* hybridization (FISH) may be correlated with other physical and genetic map data (Heinz-Ulrich, et al. (1995) in Meyers, *supra*, pp. 965-968). Examples of genetic map data can be found in various scientific journals or at the Online Mendelian Inheritance in Man (OMIM) World Wide Web site. Correlation between the location of the gene encoding MDDT on a physical map and a specific disorder, or a predisposition to a specific disorder, may help define the region of DNA associated with that disorder and thus may further positional cloning efforts.

*In situ* hybridization of chromosomal preparations and physical mapping techniques, such as linkage analysis using established chromosomal markers, may be used for extending genetic maps. Often the placement of a gene on the chromosome of another mammalian species, such as mouse, may reveal associated markers even if the exact chromosomal locus is not known. This information is valuable to investigators searching for disease genes using positional cloning or other gene discovery techniques. Once the gene or genes responsible for a disease or syndrome have been crudely localized by genetic linkage to a particular genomic region, e.g., ataxia-telangiectasia to 11q22-23, any sequences mapping to that area may represent associated or regulatory genes for further

investigation (Gatti, R.A. et al. (1988) Nature 336:577-580). The nucleotide sequence of the instant invention may also be used to detect differences in the chromosomal location due to translocation, inversion, etc., among normal, carrier, or affected individuals.

In another embodiment of the invention, MDDT, its catalytic or immunogenic fragments, or oligopeptides thereof can be used for screening libraries of compounds in any of a variety of drug screening techniques. The fragment employed in such screening may be free in solution, affixed to a solid support, borne on a cell surface, or located intracellularly. The formation of binding complexes between MDDT and the agent being tested may be measured.

Another technique for drug screening provides for high throughput screening of compounds having suitable binding affinity to the protein of interest (Geysen, et al. (1984) PCT application WO84/03564). In this method, large numbers of different small test compounds are synthesized on a solid substrate. The test compounds are reacted with MDDT, or fragments thereof, and washed. Bound MDDT is then detected by methods well known in the art. Purified MDDT can also be coated directly onto plates for use in the aforementioned drug screening techniques. Alternatively, non-neutralizing antibodies can be used to capture the peptide and immobilize it on a solid support.

In another embodiment, one may use competitive drug screening assays in which neutralizing antibodies capable of binding MDDT specifically compete with a test compound for binding MDDT. In this manner, antibodies can be used to detect the presence of any peptide which shares one or more antigenic determinants with MDDT.

In additional embodiments, the nucleotide sequences which encode MDDT may be used in any molecular biology techniques that have yet to be developed, provided the new techniques rely on properties of nucleotide sequences that are currently known, including, but not limited to, such properties as the triplet genetic code and specific base pair interactions.

Without further elaboration, it is believed that one skilled in the art can, using the preceding description, utilize the present invention to its fullest extent. The following embodiments are, therefore, to be construed as merely illustrative, and not limitative of the remainder of the disclosure in any way whatsoever.

The disclosures of all patents, applications and publications, mentioned above and below, in particular U.S. Ser. No. 60/304,298, U.S. Ser. No. 60/305,324, U.S. Ser. No. 60/307,003, U.S. Ser. No. 60/308,185, U.S. Ser. No. 60/310,096, U.S. Ser. No. 60/311,551 and U.S. Ser. No. 60/363,649, are expressly incorporated by reference herein.

## EXAMPLES

### I. Construction of cDNA Libraries

Incyte cDNAs were derived from cDNA libraries described in the LIFESEQ GOLD database

(Incyte Genomics, Palo Alto CA). Some tissues were homogenized and lysed in guanidinium isothiocyanate, while others were homogenized and lysed in phenol or in a suitable mixture of denaturants, such as TRIZOL (Invitrogen), a monophasic solution of phenol and guanidine isothiocyanate. The resulting lysates were centrifuged over CsCl cushions or extracted with  
5 chloroform. RNA was precipitated from the lysates with either isopropanol or sodium acetate and ethanol, or by other routine methods.

Phenol extraction and precipitation of RNA were repeated as necessary to increase RNA purity. In some cases, RNA was treated with DNase. For most libraries, poly(A)+ RNA was isolated using oligo d(T)-coupled paramagnetic particles (Promega), OLIGOTEX latex particles (QIAGEN,  
10 Chatsworth CA), or an OLIGOTEX mRNA purification kit (QIAGEN). Alternatively, RNA was isolated directly from tissue lysates using other RNA isolation kits, e.g., the POLY(A)PURE mRNA purification kit (Ambion, Austin TX).

In some cases, Stratagene was provided with RNA and constructed the corresponding cDNA libraries. Otherwise, cDNA was synthesized and cDNA libraries were constructed with the UNIZAP  
15 vector system (Stratagene) or SUPERScript plasmid system (Invitrogen), using the recommended procedures or similar methods known in the art (Ausubel et al., *supra*, ch. 5). Reverse transcription was initiated using oligo d(T) or random primers. Synthetic oligonucleotide adapters were ligated to double stranded cDNA, and the cDNA was digested with the appropriate restriction enzyme or enzymes. For most libraries, the cDNA was size-selected (300-1000 bp) using SEPHACRYL S1000,  
20 SEPHAROSE CL2B, or SEPHAROSE CL4B column chromatography (Amersham Biosciences) or preparative agarose gel electrophoresis. cDNAs were ligated into compatible restriction enzyme sites of the polylinker of a suitable plasmid, e.g., PBLUESCRIPT plasmid (Stratagene), PSPO1 plasmid (Invitrogen), PCDNA2.1 plasmid (Invitrogen, Carlsbad CA), PBK-CMV plasmid (Stratagene), PCR2-TOPOTA plasmid (Invitrogen), PCMV-ICIS plasmid (Stratagene), pIGEN (Incyte Genomics, Palo  
25 Alto CA), pRARE (Incyte Genomics), or pINCY (Incyte Genomics), or derivatives thereof. Recombinant plasmids were transformed into competent *E. coli* cells including XL1-Blue, XL1-BlueMRF, or SOLR from Stratagene or DH5 $\alpha$ , DH10B, or ElectroMAX DH10B from Invitrogen.

## II. Isolation of cDNA Clones

Plasmids obtained as described in Example I were recovered from host cells by *in vivo*  
30 excision using the UNIZAP vector system (Stratagene) or by cell lysis. Plasmids were purified using at least one of the following: a Magic or WIZARD Minipreps DNA purification system (Promega); an AGTC Miniprep purification kit (Edge Biosystems, Gaithersburg MD); and QIAWELL 8 Plasmid, QIAWELL 8 Plus Plasmid, QIAWELL 8 Ultra Plasmid purification systems or the R.E.A.L. PREP 96 plasmid purification kit from QIAGEN. Following precipitation, plasmids were resuspended in 0.1  
35 ml of distilled water and stored, with or without lyophilization, at 4°C.

Alternatively, plasmid DNA was amplified from host cell lysates using direct link PCR in a high-throughput format (Rao, V.B. (1994) Anal. Biochem. 216:1-14). Host cell lysis and thermal cycling steps were carried out in a single reaction mixture. Samples were processed and stored in 384-well plates, and the concentration of amplified plasmid DNA was quantified fluorometrically using PICOGREEN dye (Molecular Probes, Eugene OR) and a FLUOROSKAN II fluorescence scanner (Labsystems Oy, Helsinki, Finland).

### III. Sequencing and Analysis

Incyte cDNA recovered in plasmids as described in Example II were sequenced as follows.

Sequencing reactions were processed using standard methods or high-throughput instrumentation such as the ABI CATALYST 800 (Applied Biosystems) thermal cycler or the PTC-200 thermal cycler (MJ Research) in conjunction with the HYDRA microdispenser (Robbins Scientific) or the MICROLAB 2200 (Hamilton) liquid transfer system. cDNA sequencing reactions were prepared using reagents provided by Amersham Biosciences or supplied in ABI sequencing kits such as the ABI PRISM BIGDYE Terminator cycle sequencing ready reaction kit (Applied Biosystems).

Electrophoretic separation of cDNA sequencing reactions and detection of labeled polynucleotides were carried out using the MEGABACE 1000 DNA sequencing system (Amersham Biosciences); the ABI PRISM 373 or 377 sequencing system (Applied Biosystems) in conjunction with standard ABI protocols and base calling software; or other sequence analysis systems known in the art. Reading frames within the cDNA sequences were identified using standard methods (Ausubel et al., *supra*, ch. 7). Some of the cDNA sequences were selected for extension using the techniques disclosed in Example VIII.

The polynucleotide sequences derived from Incyte cDNAs were validated by removing vector, linker, and poly(A) sequences and by masking ambiguous bases, using algorithms and programs based on BLAST, dynamic programming, and dinucleotide nearest neighbor analysis. The Incyte cDNA sequences or translations thereof were then queried against a selection of public databases such as the GenBank primate, rodent, mammalian, vertebrate, and eukaryote databases, and BLOCKS, PRINTS, DOMO, PRODOM; PROTEOME databases with sequences from *Homo sapiens*, *Rattus norvegicus*, *Mus musculus*, *Caenorhabditis elegans*, *Saccharomyces cerevisiae*, *Schizosaccharomyces pombe*, and *Candida albicans* (Incyte Genomics, Palo Alto CA); hidden Markov model (HMM)-based protein family databases such as PFAM, INCY, and TIGRFAM (Haft, D.H. et al. (2001) Nucleic Acids Res. 29:41-43); and HMM-based protein domain databases such as SMART (Schultz, J. et al. (1998) Proc. Natl. Acad. Sci. USA 95:5857-5864; Letunic, I. et al. (2002) Nucleic Acids Res. 30:242-244). (HMM is a probabilistic approach which analyzes consensus primary structures of gene families; see, for example, Eddy, S.R. (1996) Curr. Opin. Struct. Biol. 6:361-365.) The queries were performed using programs based on BLAST, FASTA, BLIMPS, and

HMMER. The Incyte cDNA sequences were assembled to produce full length polynucleotide sequences. Alternatively, GenBank cDNAs, GenBank ESTs, stitched sequences, stretched sequences, or Genscan-predicted coding sequences (see Examples IV and V) were used to extend Incyte cDNA assemblages to full length. Assembly was performed using programs based on Phred, Phrap, and Consed, and cDNA assemblages were screened for open reading frames using programs based on GeneMark, BLAST, and FASTA. The full length polynucleotide sequences were translated to derive the corresponding full length polypeptide sequences. Alternatively, a polypeptide may begin at any of the methionine residues of the full length translated polypeptide. Full length polypeptide sequences were subsequently analyzed by querying against databases such as the GenBank protein databases (genpept), SwissProt, the PROTEOME databases, BLOCKS, PRINTS, DOMO, PRODOM, Prosite, hidden Markov model (HMM)-based protein family databases such as PFAM, INCY, and TIGRFAM; and HMM-based protein domain databases such as SMART. Full length polynucleotide sequences are also analyzed using MACDNASIS PRO software (Hitachi Software Engineering, South San Francisco CA) and LASERGENE software (DNASTAR). Polynucleotide and polypeptide sequence alignments are generated using default parameters specified by the CLUSTAL algorithm as incorporated into the MEGALIGN multisequence alignment program (DNASTAR), which also calculates the percent identity between aligned sequences.

Table 7 summarizes the tools, programs, and algorithms used for the analysis and assembly of Incyte cDNA and full length sequences and provides applicable descriptions, references, and threshold parameters. The first column of Table 7 shows the tools, programs, and algorithms used, the second column provides brief descriptions thereof, the third column presents appropriate references, all of which are incorporated by reference herein in their entirety, and the fourth column presents, where applicable, the scores, probability values, and other parameters used to evaluate the strength of a match between two sequences (the higher the score or the lower the probability value, the greater the identity between two sequences).

The programs described above for the assembly and analysis of full length polynucleotide and polypeptide sequences were also used to identify polynucleotide sequence fragments from SEQ ID NO:57-112. Fragments from about 20 to about 4000 nucleotides which are useful in hybridization and amplification technologies are described in Table 4, column 2.

#### IV. Identification and Editing of Coding Sequences from Genomic DNA

Putative molecules for disease detection and treatment were initially identified by running the Genscan gene identification program against public genomic sequence databases (e.g., gbpr and gbhtg). Genscan is a general-purpose gene identification program which analyzes genomic DNA sequences from a variety of organisms (Burge, C. and S. Karlin (1997) J. Mol. Biol. 268:78-94; Burge, C. and S. Karlin (1998) Curr. Opin. Struct. Biol. 8:346-354). The program concatenates

predicted exons to form an assembled cDNA sequence extending from a methionine to a stop codon. The output of Genscan is a FASTA database of polynucleotide and polypeptide sequences. The maximum range of sequence for Genscan to analyze at once was set to 30 kb. To determine which of these Genscan predicted cDNA sequences encode molecules for disease detection and treatment, the encoded polypeptides were analyzed by querying against PFAM models for molecules for disease detection and treatment. Potential molecules for disease detection and treatment were also identified by homology to Incyte cDNA sequences that had been annotated as molecules for disease detection and treatment. These selected Genscan-predicted sequences were then compared by BLAST analysis to the genpept and gbpi public databases. Where necessary, the Genscan-predicted sequences were then edited by comparison to the top BLAST hit from genpept to correct errors in the sequence predicted by Genscan, such as extra or omitted exons. BLAST analysis was also used to find any Incyte cDNA or public cDNA coverage of the Genscan-predicted sequences, thus providing evidence for transcription. When Incyte cDNA coverage was available, this information was used to correct or confirm the Genscan predicted sequence. Full length polynucleotide sequences were obtained by assembling Genscan-predicted coding sequences with Incyte cDNA sequences and/or public cDNA sequences using the assembly process described in Example III. Alternatively, full length polynucleotide sequences were derived entirely from edited or unedited Genscan-predicted coding sequences.

#### V. Assembly of Genomic Sequence Data with cDNA Sequence Data

##### 20 "Stitched" Sequences

Partial cDNA sequences were extended with exons predicted by the Genscan gene identification program described in Example IV. Partial cDNAs assembled as described in Example III were mapped to genomic DNA and parsed into clusters containing related cDNAs and Genscan exon predictions from one or more genomic sequences. Each cluster was analyzed using an algorithm based on graph theory and dynamic programming to integrate cDNA and genomic information, generating possible splice variants that were subsequently confirmed, edited, or extended to create a full length sequence. Sequence intervals in which the entire length of the interval was present on more than one sequence in the cluster were identified, and intervals thus identified were considered to be equivalent by transitivity. For example, if an interval was present on a cDNA and two genomic sequences, then all three intervals were considered to be equivalent. This process allows unrelated but consecutive genomic sequences to be brought together, bridged by cDNA sequence. Intervals thus identified were then "stitched" together by the stitching algorithm in the order that they appear along their parent sequences to generate the longest possible sequence, as well as sequence variants. Linkages between intervals which proceed along one type of parent sequence (cDNA to cDNA or genomic sequence to genomic sequence) were given preference over linkages which change parent



type (cDNA to genomic sequence). The resultant stitched sequences were translated and compared by BLAST analysis to the genpept and gbpr public databases. Incorrect exons predicted by Genscan were corrected by comparison to the top BLAST hit from genpept. Sequences were further extended with additional cDNA sequences, or by inspection of genomic DNA, when necessary.

## 5 **"Stretched" Sequences**

Partial DNA sequences were extended to full length with an algorithm based on BLAST analysis. First, partial cDNAs assembled as described in Example III were queried against public databases such as the GenBank primate, rodent, mammalian, vertebrate, and eukaryote databases using the BLAST program. The nearest GenBank protein homolog was then compared by BLAST  
10 analysis to either Incyte cDNA sequences or GenScan exon predicted sequences described in Example IV. A chimeric protein was generated by using the resultant high-scoring segment pairs (HSPs) to map the translated sequences onto the GenBank protein homolog. Insertions or deletions may occur in the chimeric protein with respect to the original GenBank protein homolog. The GenBank protein homolog, the chimeric protein, or both were used as probes to search for  
15 homologous genomic sequences from the public human genome databases. Partial DNA sequences were therefore "stretched" or extended by the addition of homologous genomic sequences. The resultant stretched sequences were examined to determine whether it contained a complete gene.

## **VI. Chromosomal Mapping of MDDT Encoding Polynucleotides**

The sequences which were used to assemble SEQ ID NO:57-112 were compared with  
20 sequences from the Incyte LIFESEQ database and public domain databases using BLAST and other implementations of the Smith-Waterman algorithm. Sequences from these databases that matched SEQ ID NO:57-112 were assembled into clusters of contiguous and overlapping sequences using assembly algorithms such as Phrap (Table 7). Radiation hybrid and genetic mapping data available from public resources such as the Stanford Human Genome Center (SHGC), Whitehead Institute for  
25 Genome Research (WIGR), and Généthon were used to determine if any of the clustered sequences had been previously mapped. Inclusion of a mapped sequence in a cluster resulted in the assignment of all sequences of that cluster, including its particular SEQ ID NO:, to that map location.

Map locations are represented by ranges, or intervals, of human chromosomes. The map position of an interval, in centiMorgans, is measured relative to the terminus of the chromosome's p-arm. (The centiMorgan (cM) is a unit of measurement based on recombination frequencies between  
30 chromosomal markers. On average, 1 cM is roughly equivalent to 1 megabase (Mb) of DNA in humans, although this can vary widely due to hot and cold spots of recombination.) The cM distances are based on genetic markers mapped by Généthon which provide boundaries for radiation hybrid markers whose sequences were included in each of the clusters. Human genome maps and  
35 other resources available to the public, such as the NCBI "GeneMap'99" World Wide Web site

(<http://www.ncbi.nlm.nih.gov/genemap/>), can be employed to determine if previously identified disease genes map within or in proximity to the intervals indicated above.

## VII. Analysis of Polynucleotide Expression

Northern analysis is a laboratory technique used to detect the presence of a transcript of a gene and involves the hybridization of a labeled nucleotide sequence to a membrane on which RNAs from a particular cell type or tissue have been bound (Sambrook, *supra*, ch. 7; Ausubel et al., *supra*, ch. 4).

Analogous computer techniques applying BLAST were used to search for identical or related molecules in cDNA databases such as GenBank or LIFESEQ (Incyte Genomics). This analysis is much faster than multiple membrane-based hybridizations. In addition, the sensitivity of the computer search can be modified to determine whether any particular match is categorized as exact or similar. The basis of the search is the product score, which is defined as:

$$\frac{\text{BLAST Score} \times \text{Percent Identity}}{5 \times \text{minimum \{length(Seq. 1), length(Seq. 2)\}}}$$

The product score takes into account both the degree of similarity between two sequences and the length of the sequence match. The product score is a normalized value between 0 and 100, and is calculated as follows: the BLAST score is multiplied by the percent nucleotide identity and the product is divided by (5 times the length of the shorter of the two sequences). The BLAST score is calculated by assigning a score of +5 for every base that matches in a high-scoring segment pair (HSP), and -4 for every mismatch. Two sequences may share more than one HSP (separated by gaps). If there is more than one HSP, then the pair with the highest BLAST score is used to calculate the product score. The product score represents a balance between fractional overlap and quality in a BLAST alignment. For example, a product score of 100 is produced only for 100% identity over the entire length of the shorter of the two sequences being compared. A product score of 70 is produced either by 100% identity and 70% overlap at one end, or by 88% identity and 100% overlap at the other. A product score of 50 is produced either by 100% identity and 50% overlap at one end, or 79% identity and 100% overlap.

Alternatively, polynucleotides encoding MDDT are analyzed with respect to the tissue sources from which they were derived. For example, some full length sequences are assembled, at least in part, with overlapping Incyte cDNA sequences (see Example III). Each cDNA sequence is derived from a cDNA library constructed from a human tissue. Each human tissue is classified into one of the following organ/tissue categories: cardiovascular system; connective tissue; digestive system; embryonic structures; endocrine system; exocrine glands; genitalia, female; genitalia, male;

germ cells; hemic and immune system; liver; musculoskeletal system; nervous system; pancreas; respiratory system; sense organs; skin; stomatognathic system; unclassified/mixed; or urinary tract.

The number of libraries in each category is counted and divided by the total number of libraries across all categories. Similarly, each human tissue is classified into one of the following

- 5 disease/condition categories: cancer, cell line, developmental, inflammation, neurological, trauma, cardiovascular, pooled, and other, and the number of libraries in each category is counted and divided by the total number of libraries across all categories. The resulting percentages reflect the tissue- and disease-specific expression of cDNA encoding MDDT. cDNA sequences and cDNA library/tissue information are found in the LIFESEQ GOLD database (Incyte Genomics, Palo Alto CA).

10 **VIII. Extension of MDDT Encoding Polynucleotides**

- Full length polynucleotides are produced by extension of an appropriate fragment of the full length molecule using oligonucleotide primers designed from this fragment. One primer was synthesized to initiate 5' extension of the known fragment, and the other primer was synthesized to initiate 3' extension of the known fragment. The initial primers were designed using OLIGO 4.06  
15 software (National Biosciences), or another appropriate program, to be about 22 to 30 nucleotides in length, to have a GC content of about 50% or more, and to anneal to the target sequence at temperatures of about 68°C to about 72°C. Any stretch of nucleotides which would result in hairpin structures and primer-primer dimerizations was avoided.

- Selected human cDNA libraries were used to extend the sequence. If more than one  
20 extension was necessary or desired, additional or nested sets of primers were designed.

- High fidelity amplification was obtained by PCR using methods well known in the art. PCR was performed in 96-well plates using the PTC-200 thermal cycler (MJ Research, Inc.). The reaction mix contained DNA template, 200 nmol of each primer, reaction buffer containing  $Mg^{2+}$ ,  $(NH_4)_2SO_4$ , and 2-mercaptoethanol, Taq DNA polymerase (Amersham Biosciences), ELONGASE enzyme  
25 (Invitrogen), and Pfu DNA polymerase (Stratagene), with the following parameters for primer pair PCI A and PCI B: Step 1: 94°C, 3 min; Step 2: 94°C, 15 sec; Step 3: 60°C, 1 min; Step 4: 68°C, 2 min; Step 5: Steps 2, 3, and 4 repeated 20 times; Step 6: 68°C, 5 min; Step 7: storage at 4°C. In the alternative, the parameters for primer pair T7 and SK+ were as follows: Step 1: 94°C, 3 min; Step 2: 94°C, 15 sec; Step 3: 57°C, 1 min; Step 4: 68°C, 2 min; Step 5: Steps 2, 3, and 4 repeated 20 times;  
30 Step 6: 68°C, 5 min; Step 7: storage at 4°C.

- The concentration of DNA in each well was determined by dispensing 100  $\mu$ l PICOGREEN quantitation reagent (0.25% (v/v) PICOGREEN; Molecular Probes, Eugene OR) dissolved in 1X TE and 0.5  $\mu$ l of undiluted PCR product into each well of an opaque fluorimeter plate (Corning Costar, Acton MA), allowing the DNA to bind to the reagent. The plate was scanned in a Fluoroskan II  
35 (Labsystems Oy, Helsinki, Finland) to measure the fluorescence of the sample and to quantify the

concentration of DNA. A 5  $\mu$ l to 10  $\mu$ l aliquot of the reaction mixture was analyzed by electrophoresis on a 1 % agarose gel to determine which reactions were successful in extending the sequence.

The extended nucleotides were desalted and concentrated, transferred to 384-well plates, 5 digested with CviJI cholera virus endonuclease (Molecular Biology Research, Madison WI), and sonicated or sheared prior to religation into pUC 18 vector (Amersham Biosciences). For shotgun sequencing, the digested nucleotides were separated on low concentration (0.6 to 0.8%) agarose gels, fragments were excised, and agar digested with Agar ACE (Promega). Extended clones were religated using T4 ligase (New England Biolabs, Beverly MA) into pUC 18 vector (Amersham 10 Biosciences), treated with Pfu DNA polymerase (Stratagene) to fill-in restriction site overhangs, and transfected into competent *E. coli* cells. Transformed cells were selected on antibiotic-containing media, and individual colonies were picked and cultured overnight at 37°C in 384-well plates in LB/2x carb liquid media.

The cells were lysed, and DNA was amplified by PCR using Taq DNA polymerase 15 (Amersham Biosciences) and Pfu DNA polymerase (Stratagene) with the following parameters: Step 1: 94°C, 3 min; Step 2: 94°C, 15 sec; Step 3: 60°C, 1 min; Step 4: 72°C, 2 min; Step 5: steps 2, 3, and 4 repeated 29 times; Step 6: 72°C, 5 min; Step 7: storage at 4°C. DNA was quantified by PICOGREEN reagent (Molecular Probes) as described above. Samples with low DNA recoveries were reamplified using the same conditions as described above. Samples were diluted with 20% 20 dimethylsulfoxide (1:2, v/v), and sequenced using DYENAMIC energy transfer sequencing primers and the DYENAMIC DIRECT kit (Amersham Biosciences) or the ABI PRISM BIGDYE Terminator cycle sequencing ready reaction kit (Applied Biosystems).

In like manner, full length polynucleotides are verified using the above procedure or are used to obtain 5' regulatory sequences using the above procedure along with oligonucleotides designed for 25 such extension, and an appropriate genomic library.

#### **IX. Identification of Single Nucleotide Polymorphisms in MDDT Encoding Polynucleotides**

Common DNA sequence variants known as single nucleotide polymorphisms (SNPs) were identified in SEQ ID NO:57-112 using the LIFESEQ database (Incyte Genomics). Sequences from the same gene were clustered together and assembled as described in Example III, allowing the 30 identification of all sequence variants in the gene. An algorithm consisting of a series of filters was used to distinguish SNPs from other sequence variants. Preliminary filters removed the majority of basecall errors by requiring a minimum Phred quality score of 15, and removed sequence alignment errors and errors resulting from improper trimming of vector sequences, chimeras, and splice variants. An automated procedure of advanced chromosome analysis analysed the original 35 chromatogram files in the vicinity of the putative SNP. Clone error filters used statistically generated

algorithms to identify errors introduced during laboratory processing, such as those caused by reverse transcriptase, polymerase, or somatic mutation. Clustering error filters used statistically generated algorithms to identify errors resulting from clustering of close homologs or pseudogenes, or due to contamination by non-human sequences. A final set of filters removed duplicates and SNPs found in  
5 immunoglobulins or T-cell receptors.

Certain SNPs were selected for further characterization by mass spectrometry using the high throughput MASSARRAY system (Sequenom, Inc.) to analyze allele frequencies at the SNP sites in four different human populations. The Caucasian population comprised 92 individuals (46 male, 46 female), including 83 from Utah, four French, three Venezuelan, and two Amish individuals. The  
10 African population comprised 194 individuals (97 male, 97 female), all African Americans. The Hispanic population comprised 324 individuals (162 male, 162 female), all Mexican Hispanic. The Asian population comprised 126 individuals (64 male, 62 female) with a reported parental breakdown of 43% Chinese, 31% Japanese, 13% Korean, 5% Vietnamese, and 8% other Asian. Allele frequencies were first analyzed in the Caucasian population; in some cases those SNPs which showed  
15 no allelic variance in this population were not further tested in the other three populations.

#### **X. Labeling and Use of Individual Hybridization Probes**

Hybridization probes derived from SEQ ID NO:57-112 are employed to screen cDNAs, genomic DNAs, or mRNAs. Although the labeling of oligonucleotides, consisting of about 20 base pairs, is specifically described, essentially the same procedure is used with larger nucleotide  
20 fragments. Oligonucleotides are designed using state-of-the-art software such as OLIGO 4.06 software (National Biosciences) and labeled by combining 50 pmol of each oligomer, 250  $\mu$ Ci of [ $\gamma$ - $^{32}$ P] adenosine triphosphate (Amersham Biosciences), and T4 polynucleotide kinase (DuPont NEN, Boston MA). The labeled oligonucleotides are substantially purified using a SEPHADEX G-25 superfine size exclusion dextran bead column (Amersham Biosciences). An aliquot containing 10<sup>7</sup>  
25 counts per minute of the labeled probe is used in a typical membrane-based hybridization analysis of human genomic DNA digested with one of the following endonucleases: Ase I, Bgl II, Eco RI, Pst I, Xba I, or Pvu II (DuPont NEN).

The DNA from each digest is fractionated on a 0.7% agarose gel and transferred to nylon membranes (Nytran Plus, Schleicher & Schuell, Durham NH). Hybridization is carried out for 16  
30 hours at 40°C. To remove nonspecific signals, blots are sequentially washed at room temperature under conditions of up to, for example, 0.1 x saline sodium citrate and 0.5% sodium dodecyl sulfate. Hybridization patterns are visualized using autoradiography or an alternative imaging means and compared.

#### **XI. Microarrays**

35 The linkage or synthesis of array elements upon a microarray can be achieved utilizing

photolithography, piezoelectric printing (ink-jet printing; see, e.g., Baldeschweiler et al., *supra*), mechanical microspotting technologies, and derivatives thereof. The substrate in each of the aforementioned technologies should be uniform and solid with a non-porous surface (Schena, M., ed. (1999) DNA Microarrays: A Practical Approach, Oxford University Press, London). Suggested

5 substrates include silicon, silica, glass slides, glass chips, and silicon wafers. Alternatively, a procedure analogous to a dot or slot blot may also be used to arrange and link elements to the surface of a substrate using thermal, UV, chemical, or mechanical bonding procedures. A typical array may be produced using available methods and machines well known to those of ordinary skill in the art and may contain any appropriate number of elements (Schena, M. et al. (1995) *Science* 270:467-470;

10 Shalon, D. et al. (1996) *Genome Res.* 6:639-645; Marshall, A. and J. Hodgson (1998) *Nat. Biotechnol.* 16:27-31).

Full length cDNAs, Expressed Sequence Tags (ESTs), or fragments or oligomers thereof may comprise the elements of the microarray. Fragments or oligomers suitable for hybridization can be selected using software well known in the art such as LASERGENE software (DNASTAR). The

15 array elements are hybridized with polynucleotides in a biological sample. The polynucleotides in the biological sample are conjugated to a fluorescent label or other molecular tag for ease of detection. After hybridization, nonhybridized nucleotides from the biological sample are removed, and a fluorescence scanner is used to detect hybridization at each array element. Alternatively, laser desorption and mass spectrometry may be used for detection of hybridization. The degree of

20 complementarity and the relative abundance of each polynucleotide which hybridizes to an element on the microarray may be assessed. In one embodiment, microarray preparation and usage is described in detail below.

#### **Tissue or Cell Sample Preparation**

Total RNA is isolated from tissue samples using the guanidinium thiocyanate method and

25 poly(A)<sup>+</sup> RNA is purified using the oligo-(dT) cellulose method. Each poly(A)<sup>+</sup> RNA sample is reverse transcribed using MMLV reverse-transcriptase, 0.05 pg/ $\mu$ l oligo-(dT) primer (21mer), 1X first strand buffer, 0.03 units/ $\mu$ l RNase inhibitor, 500  $\mu$ M dATP, 500  $\mu$ M dGTP, 500  $\mu$ M dTTP, 40  $\mu$ M dCTP, 40  $\mu$ M dCTP-Cy3 (BDS) or dCTP-Cy5 (Amersham Biosciences). The reverse transcription reaction is performed in a 25 ml volume containing 200 ng poly(A)<sup>+</sup> RNA with

30 GEMBRIGHT kits (Incyte). Specific control poly(A)<sup>+</sup> RNAs are synthesized by *in vitro* transcription from non-coding yeast genomic DNA. After incubation at 37°C for 2 hr, each reaction sample (one with Cy3 and another with Cy5 labeling) is treated with 2.5 ml of 0.5M sodium hydroxide and incubated for 20 minutes at 85°C to stop the reaction and degrade the RNA. Samples are purified using two successive CHROMA SPIN 30 gel filtration spin columns (CLONTECH Laboratories, Inc.

35 (CLONTECH), Palo Alto CA) and after combining, both reaction samples are ethanol precipitated

using 1 ml of glycogen (1 mg/ml), 60 ml sodium acetate, and 300 ml of 100% ethanol. The sample is then dried to completion using a SpeedVAC (Savant Instruments Inc., Holbrook NY) and resuspended in 14  $\mu$ l 5X SSC/0.2% SDS.

#### Microarray Preparation

- 5       Sequences of the present invention are used to generate array elements. Each array element is amplified from bacterial cells containing vectors with cloned cDNA inserts. PCR amplification uses primers complementary to the vector sequences flanking the cDNA insert. Array elements are amplified in thirty cycles of PCR from an initial quantity of 1-2 ng to a final quantity greater than 5  $\mu$ g. Amplified array elements are then purified using SEPHACRYL-400 (Amersham Biosciences).
- 10       Purified array elements are immobilized on polymer-coated glass slides. Glass microscope slides (Corning) are cleaned by ultrasound in 0.1% SDS and acetone, with extensive distilled water washes between and after treatments. Glass slides are etched in 4% hydrofluoric acid (VWR Scientific Products Corporation (VWR), West Chester PA), washed extensively in distilled water, and coated with 0.05% aminopropyl silane (Sigma) in 95% ethanol. Coated slides are cured in a
- 15       110°C oven.

Array elements are applied to the coated glass substrate using a procedure described in U.S. Patent No. 5,807,522, incorporated herein by reference. 1  $\mu$ l of the array element DNA, at an average concentration of 100 ng/ $\mu$ l, is loaded into the open capillary printing element by a high-speed robotic apparatus. The apparatus then deposits about 5 nl of array element sample per slide.

- 20       Microarrays are UV-crosslinked using a STRATALINKER UV-crosslinker (Stratagene). Microarrays are washed at room temperature once in 0.2% SDS and three times in distilled water. Non-specific binding sites are blocked by incubation of microarrays in 0.2% casein in phosphate buffered saline (PBS) (Tropix, Inc., Bedford MA) for 30 minutes at 60°C followed by washes in 0.2% SDS and distilled water as before.

#### 25       Hybridization

- Hybridization reactions contain 9  $\mu$ l of sample mixture consisting of 0.2  $\mu$ g each of Cy3 and Cy5 labeled cDNA synthesis products in 5X SSC, 0.2% SDS hybridization buffer. The sample mixture is heated to 65°C for 5 minutes and is aliquoted onto the microarray surface and covered with an 1.8 cm<sup>2</sup> coverslip. The arrays are transferred to a waterproof chamber having a cavity just
- 30       slightly larger than a microscope slide. The chamber is kept at 100% humidity internally by the addition of 140  $\mu$ l of 5X SSC in a corner of the chamber. The chamber containing the arrays is incubated for about 6.5 hours at 60°C. The arrays are washed for 10 min at 45°C in a first wash buffer (1X SSC, 0.1% SDS), three times for 10 minutes each at 45°C in a second wash buffer (0.1X SSC), and dried.

#### 35       Detection

Reporter-labeled hybridization complexes are detected with a microscope equipped with an Innova 70 mixed gas 10 W laser (Coherent, Inc., Santa Clara CA) capable of generating spectral lines at 488 nm for excitation of Cy3 and at 632 nm for excitation of Cy5. The excitation laser light is focused on the array using a 20X microscope objective (Nikon, Inc., Melville NY). The slide  
5 containing the array is placed on a computer-controlled X-Y stage on the microscope and raster-scanned past the objective. The 1.8 cm x 1.8 cm array used in the present example is scanned with a resolution of 20 micrometers.

In two separate scans, a mixed gas multiline laser excites the two fluorophores sequentially. Emitted light is split, based on wavelength, into two photomultiplier tube detectors (PMT R1477,  
10 Hamamatsu Photonics Systems, Bridgewater NJ) corresponding to the two fluorophores. Appropriate filters positioned between the array and the photomultiplier tubes are used to filter the signals. The emission maxima of the fluorophores used are 565 nm for Cy3 and 650 nm for Cy5. Each array is typically scanned twice, one scan per fluorophore using the appropriate filters at the laser source, although the apparatus is capable of recording the spectra from both fluorophores simultaneously.

15 The sensitivity of the scans is typically calibrated using the signal intensity generated by a cDNA control species added to the sample mixture at a known concentration. A specific location on the array contains a complementary DNA sequence, allowing the intensity of the signal at that location to be correlated with a weight ratio of hybridizing species of 1:100,000. When two samples from different sources (e.g., representing test and control cells), each labeled with a different  
20 fluorophore, are hybridized to a single array for the purpose of identifying genes that are differentially expressed, the calibration is done by labeling samples of the calibrating cDNA with the two fluorophores and adding identical amounts of each to the hybridization mixture.

The output of the photomultiplier tube is digitized using a 12-bit RTI-835H analog-to-digital (A/D) conversion board (Analog Devices, Inc., Norwood MA) installed in an IBM-compatible PC  
25 computer. The digitized data are displayed as an image where the signal intensity is mapped using a linear 20-color transformation to a pseudocolor scale ranging from blue (low signal) to red (high signal). The data is also analyzed quantitatively. Where two different fluorophores are excited and measured simultaneously, the data are first corrected for optical crosstalk (due to overlapping emission spectra) between the fluorophores using each fluorophore's emission spectrum.

30 A grid is superimposed over the fluorescence signal image such that the signal from each spot is centered in each element of the grid. The fluorescence signal within each element is then integrated to obtain a numerical value corresponding to the average intensity of the signal. The software used for signal analysis is the GEMTOOLS gene expression analysis program (Incyte). Array elements that exhibited at least about a two-fold change in expression, a signal-to-background  
35 ratio of at least 2.5, and an element spot size of at least 40% were identified as differentially



expressed using the GEMTOOLS program (Incyte Genomics).

#### Expression

For example, SEQ ID NO:58 was downregulated by at least two-fold in five out of the eight endothelial cell lines treated with 10ng/ml TNF- $\alpha$  within four hours. SEQ ID NO:58 was also downregulated in Tangier disease fibroblasts as compared to normal controls suggesting that SEQ ID NO:58, encoding SEQ ID NO:2, can be used for the diagnosis, prognosis or treatment of a cardiovascular disorder such as arteriovenous fistula, atherosclerosis, hypertension, vasculitis, Raynaud's disease, aneurysms, arterial dissections, varicose veins, thrombophlebitis and phlebothrombosis, vascular tumors, and complications of thrombolysis, balloon angioplasty, vascular replacement, coronary artery bypass, congestive heart failure, ischemic heart disease, angina pectoris, myocardial infarction, hypertensive heart disease, degenerative valvular heart disease, calcific aortic valve stenosis, congenitally bicuspid aortic valve, mitral annular calcification, mitral valve prolapse, rheumatic fever and rheumatic heart disease, infective endocarditis, nonbacterial thrombotic endocarditis, endocarditis of systemic lupus erythematosus, carcinoid heart disease, cardiomyopathy, myocarditis, pericarditis, neoplastic heart disease, congenital heart disease, complications of cardiac transplantation, congenital lung anomalies, atelectasis, pulmonary congestion and edema, pulmonary embolism, pulmonary hemorrhage, pulmonary infarction, pulmonary hypertension, vascular sclerosis, obstructive pulmonary disease, restrictive pulmonary disease, chronic obstructive pulmonary disease, emphysema, chronic bronchitis, bronchial asthma, bronchiectasis, bacterial pneumonia, viral and mycoplasmal pneumonia, lung abscess, pulmonary tuberculosis, diffuse interstitial diseases, pneumoconioses, sarcoidosis, idiopathic pulmonary fibrosis, desquamative interstitial pneumonitis, hypersensitivity pneumonitis, pulmonary eosinophilia bronchiolitis obliterans-organizing pneumonia, diffuse pulmonary hemorrhage syndromes, Goodpasture's syndromes, idiopathic pulmonary hemosiderosis, pulmonary involvement in collagen-vascular disorders, pulmonary alveolar proteinosis, lung tumors, inflammatory and noninflammatory pleural effusions, pneumothorax, pleural tumors, drug-induced lung disease, radiation-induced lung disease, and Tangier disease.

For example, SEQ ID NO:90 showed differential expression in treated versus non-treated C3A cells as determined by microarray analysis. The expression of SEQ ID NO:90 was decreased by at least two fold in C3A cells treated with 10  $\mu$ M MAH for one to six hours and with 100  $\mu$ M for one or six hours versus untreated C3A cells. SEQ ID NO:90 expression was also decreased by at least two-fold when C3A cells were treated for one to three hours with either 1  $\mu$ M, 10  $\mu$ M, or 100  $\mu$ M budesonide when compared with untreated C3A cells. These experiments indicate that SEQ ID NO:90 was significantly under-expressed in C3A cells when tested with two steroid compounds, further establishing the utility of SEQ ID NO:90 as a diagnostic marker or as a potential therapeutic target for liver disorders associated with steroid therapy such as adenomatosis, cholestasis, cirrhosis,

hemangioma, Henoch-Schonlein purpura, hepatitis, hepatocellular and metastatic carcinomas, idiopathic thrombocytopenic purpura, porphyria, sarcoidosis, and Wilson disease.

Human CD34 positive precursor cells were isolated by positive immunomagnetic selection from the leukapheresis of normal volunteer donors who had undergone G-CSF-induced stem cell mobilization. The purified CD34+ cells were cultured in vitro for 10 days in the presence of recombinant GM-CSF, Stem Cell Factor, TNF-alpha, TGF-beta1, and Flt3-Ligand. The resulting expanded cell population was enriched for cell cluster-forming immature dendritic cells (Lci) by sedimentation over a 7.5 % BSA column at 1 g for 30 min. Immature dendritic cells were cultured for two additional days in the presence of the same combination of cytokines supplemented with LPS, IL-1beta, TNF-alpha, or double strand RNA. In addition, cluster-forming immature dendritic cells were disrupted by vigorous pipetting and cultured for two additional days in the presence of the same combination of cytokines without addition of any additional factor. The partially mature dendritic cells derived by mechanical disruption of cell clusters are characterized by the presence of intracellular rod-shaped structures called Birbeck's Granules. The dendritic cell population produced using this method was called Birbeck's Granule-positive dendritic cells, or BG.

CD34+ precursor cells were compared to immature dendritic cells (Lci); Lci were compared to mature dendritic cells derived in the presence of LPS, IL-1b, TNF-alpha, or double strand RNA; and undisturbed Lci (Clusters) were compared to BG. Array elements that exhibited about at least a two-fold change in expression and a signal intensity over 250 units, a signal-to-background ratio of at least 2.5, and an element spot size of at least 40% were identified as differentially expressed using the GEMTOOLS program (Incyte Genomics). SEQ ID NO:96, which contains a GTPase activating protein motif for Arf and a Rho GAP domain, showed at least a two-fold increased expression during the differentiation of dendritic cells when induced by simple mechanical disaggregation and a greater than two-fold expression during maturation of these cells when induced by TNF-alpha. TNF-alpha is a factor produced by many cell types in response to stress. In addition, mechanical disruption is a significant stress factor during organ transplantation. Further, these experiments indicate that SEQ ID NO:96 was significantly over-expressed during differentiation and maturation of human dendritic cells, further establishing the utility of SEQ ID NO:96 as a diagnostic marker or as a potential therapeutic target for organ transplant disorders.

For example, SEQ ID NO:110 showed differential expression in diseased versus normal tissue as determined by microarray analysis. Matched normal ovary and ovarian tumor tissue samples are provided by the Huntsman Cancer Institute, (Salt Lake City, UT). The expression of MDDT was decreased in ovarian tumor cells relative to non-tumorous ovarian cells. Therefore, SEQ ID NO:110 is useful in diagnostic assays for ovarian cancer.

## **XII. Complementary Polynucleotides**

Sequences complementary to the MDDT-encoding sequences, or any parts thereof, are used to detect, decrease, or inhibit expression of naturally occurring MDDT. Although use of oligonucleotides comprising from about 15 to 30 base pairs is described, essentially the same procedure is used with smaller or with larger sequence fragments. Appropriate oligonucleotides are designed using OLIGO 4.06 software (National Biosciences) and the coding sequence of MDDT. To inhibit transcription, a complementary oligonucleotide is designed from the most unique 5' sequence and used to prevent promoter binding to the coding sequence. To inhibit translation, a complementary oligonucleotide is designed to prevent ribosomal binding to the MDDT-encoding transcript.

### 10 XIII. Expression of MDDT

Expression and purification of MDDT is achieved using bacterial or virus-based expression systems. For expression of MDDT in bacteria, cDNA is subcloned into an appropriate vector containing an antibiotic resistance gene and an inducible promoter that directs high levels of cDNA transcription. Examples of such promoters include, but are not limited to, the *trp-lac (tac)* hybrid promoter and the T5 or T7 bacteriophage promoter in conjunction with the *lac* operator regulatory element. Recombinant vectors are transformed into suitable bacterial hosts, e.g., BL21(DE3). Antibiotic resistant bacteria express MDDT upon induction with isopropyl beta-D-thiogalactopyranoside (IPTG). Expression of MDDT in eukaryotic cells is achieved by infecting insect or mammalian cell lines with recombinant *Autographica californica* nuclear polyhedrosis virus (AcMNPV), commonly known as baculovirus. The nonessential polyhedrin gene of baculovirus is replaced with cDNA encoding MDDT by either homologous recombination or bacterial-mediated transposition involving transfer plasmid intermediates. Viral infectivity is maintained and the strong polyhedrin promoter drives high levels of cDNA transcription. Recombinant baculovirus is used to infect *Spodoptera frugiperda* (Sf9) insect cells in most cases, or human hepatocytes, in some cases. Infection of the latter requires additional genetic modifications to baculovirus (Engelhard, E.K. et al. (1994) Proc. Natl. Acad. Sci. USA 91:3224-3227; Sandig, V. et al. (1996) Hum. Gene Ther. 7:1937-1945).

In most expression systems, MDDT is synthesized as a fusion protein with, e.g., glutathione S-transferase (GST) or a peptide epitope tag, such as FLAG or 6-His, permitting rapid, single-step, affinity-based purification of recombinant fusion protein from crude cell lysates. GST, a 26-kilodalton enzyme from *Schistosoma japonicum*, enables the purification of fusion proteins on immobilized glutathione under conditions that maintain protein activity and antigenicity (Amersham Biosciences). Following purification, the GST moiety can be proteolytically cleaved from MDDT at specifically engineered sites. FLAG, an 8-amino acid peptide, enables immunoaffinity purification using commercially available monoclonal and polyclonal anti-FLAG antibodies (Eastman Kodak). 6-

His, a stretch of six consecutive histidine residues, enables purification on metal-chelate resins (QIAGEN). Methods for protein expression and purification are discussed in Ausubel et al. (*supra*, ch. 10 and 16). Purified MDDT obtained by these methods can be used directly in the assays shown in Examples XVII, and XVIII where applicable.

#### 5 XIV. Functional Assays

MDDT function is assessed by expressing the sequences encoding MDDT at physiologically elevated levels in mammalian cell culture systems. cDNA is subcloned into a mammalian expression vector containing a strong promoter that drives high levels of cDNA expression. Vectors of choice include PCMV SPORT plasmid (Invitrogen, Carlsbad CA) and PCR3.1 plasmid (Invitrogen), both of which contain the cytomegalovirus promoter. 5-10  $\mu$ g of recombinant vector are transiently  
10 transfected into a human cell line, for example, an endothelial or hematopoietic cell line, using either liposome formulations or electroporation. 1-2  $\mu$ g of an additional plasmid containing sequences encoding a marker protein are co-transfected. Expression of a marker protein provides a means to distinguish transfected cells from nontransfected cells and is a reliable predictor of cDNA expression  
15 from the recombinant vector. Marker proteins of choice include, e.g., Green Fluorescent Protein (GFP; Clontech), CD64, or a CD64-GFP fusion protein. Flow cytometry (FCM), an automated, laser optics-based technique, is used to identify transfected cells expressing GFP or CD64-GFP and to evaluate the apoptotic state of the cells and other cellular properties. FCM detects and quantifies the uptake of fluorescent molecules that diagnose events preceding or coincident with cell death. These  
20 events include changes in nuclear DNA content as measured by staining of DNA with propidium iodide; changes in cell size and granularity as measured by forward light scatter and 90 degree side light scatter; down-regulation of DNA synthesis as measured by decrease in bromodeoxyuridine uptake; alterations in expression of cell surface and intracellular proteins as measured by reactivity with specific antibodies; and alterations in plasma membrane composition as measured by the binding  
25 of fluorescein-conjugated Annexin V protein to the cell surface. Methods in flow cytometry are discussed in Ormerod, M.G. (1994; Flow Cytometry, Oxford, New York NY).

The influence of MDDT on gene expression can be assessed using highly purified populations of cells transfected with sequences encoding MDDT and either CD64 or CD64-GFP. CD64 and CD64-GFP are expressed on the surface of transfected cells and bind to conserved regions  
30 of human immunoglobulin G (IgG). Transfected cells are efficiently separated from nontransfected cells using magnetic beads coated with either human IgG or antibody against CD64 (DYNAL, Lake Success NY). mRNA can be purified from the cells using methods well known by those of skill in the art. Expression of mRNA encoding MDDT and other genes of interest can be analyzed by northern analysis or microarray techniques.

#### 35 XV. Production of MDDT Specific Antibodies

MDDT substantially purified using polyacrylamide gel electrophoresis (PAGE; see, e.g., Harrington, M.G. (1990) *Methods Enzymol.* 182:488-495), or other purification techniques, is used to immunize animals (e.g., rabbits, mice, etc.) and to produce antibodies using standard protocols.

Alternatively, the MDDT amino acid sequence is analyzed using LASERGENE software (DNASTAR) to determine regions of high immunogenicity, and a corresponding oligopeptide is synthesized and used to raise antibodies by means known to those of skill in the art. Methods for selection of appropriate epitopes, such as those near the C-terminus or in hydrophilic regions are well described in the art (Ausubel et al., *supra*, ch. 11).

Typically, oligopeptides of about 15 residues in length are synthesized using an ABI 431A peptide synthesizer (Applied Biosystems) using Fmoc chemistry and coupled to KLH (Sigma-Aldrich, St. Louis MO) by reaction with N-maleimidobenzoyl-N-hydroxysuccinimide ester (MBS) to increase immunogenicity (Ausubel et al., *supra*). Rabbits are immunized with the oligopeptide-KLH complex in complete Freund's adjuvant. Resulting antisera are tested for antipeptide and anti-MDDT activity by, for example, binding the peptide or MDDT to a substrate, blocking with 1% BSA, reacting with rabbit antisera, washing, and reacting with radio-iodinated goat anti-rabbit IgG.

#### **XVI. Purification of Naturally Occurring MDDT Using Specific Antibodies**

Naturally occurring or recombinant MDDT is substantially purified by immunoaffinity chromatography using antibodies specific for MDDT. An immunoaffinity column is constructed by covalently coupling anti-MDDT antibody to an activated chromatographic resin, such as CNBr-activated SEPHAROSE (Amersham Biosciences). After the coupling, the resin is blocked and washed according to the manufacturer's instructions.

Media containing MDDT are passed over the immunoaffinity column, and the column is washed under conditions that allow the preferential absorbance of MDDT (e.g., high ionic strength buffers in the presence of detergent). The column is eluted under conditions that disrupt antibody/MDDT binding (e.g., a buffer of pH 2 to pH 3, or a high concentration of a chaotrope, such as urea or thiocyanate ion), and MDDT is collected.

#### **XVII. Identification of Molecules Which Interact with MDDT**

MDDT, or biologically active fragments thereof, are labeled with <sup>125</sup>I Bolton-Hunter reagent (Bolton, A.E. and W.M. Hunter (1973) *Biochem. J.* 133:529-539). Candidate molecules previously arrayed in the wells of a multi-well plate are incubated with the labeled MDDT, washed, and any wells with labeled MDDT complex are assayed. Data obtained using different concentrations of MDDT are used to calculate values for the number, affinity, and association of MDDT with the candidate molecules.

Alternatively, molecules interacting with MDDT are analyzed using the yeast two-hybrid system as described in Fields, S. and O. Song (1989; *Nature* 340:245-246), or using commercially

available kits based on the two-hybrid system, such as the MATCHMAKER system (Clontech).

MDDT may also be used in the PATHCALLING process (CuraGen Corp., New Haven CT) which employs the yeast two-hybrid system in a high-throughput manner to determine all interactions between the proteins encoded by two large libraries of genes (Nandabalan, K. et al. (2000) U.S.

5 Patent No. 6,057,101).

#### **XVIII. Demonstration of MDDT Activity**

Phorbol ester binding activity of MDDT is measured using an assay based on the fluorescent phorbol ester sapinotoxin-D (SAPD). Binding of SAPD to MDDT is quantified by measuring the resonance energy transfer from MDDT tryptophans to the 2-(N-methylamino)benzoyl fluorophore of  
10 the phorbol ester, as described by Slater et al. ((1996) J. Biol. Chem. 271:4627-4631).

Various modifications and variations of the described compositions, methods, and systems of the invention will be apparent to those skilled in the art without departing from the scope and spirit of the invention. It will be appreciated that the invention provides novel and useful proteins, and their  
15 encoding polynucleotides, which can be used in the drug discovery process, as well as methods for using these compositions for the detection, diagnosis, and treatment of diseases and conditions. Although the invention has been described in connection with certain embodiments, it should be understood that the invention as claimed should not be unduly limited to such specific embodiments. Nor should the description of such embodiments be considered exhaustive or limit the invention to  
20 the precise forms disclosed. Furthermore, elements from one embodiment can be readily recombined with elements from one or more other embodiments. Such combinations can form a number of embodiments within the scope of the invention. It is intended that the scope of the invention be defined by the following claims and their equivalents.

Table 1

Incyte Project ID	Polypeptide SEQ ID NO:	Incyte Polypeptide ID	Polynucleotide SEQ ID NO:	Incyte Polynucleotide ID	Incyte Full Length Clones
2867236	1	2867236CD1	57	2867236CB1	1536179CA2
1294096	2	1294096CD1	58	1294096CB1	
7238537	3	7238537CD1	59	7238537CB1	90171762CA2, 90171778CA2, 90171786CA2, 90171870CA2, 90171886CA2, 90171894CA2, 90190048CA2, 90190116CA2, 90190124CA2, 90190132CA2
7494391	4	7494391CD1	60	7494391CB1	90140260CA2
6451054	5	6451054CD1	61	6451054CB1	
7494592	6	7494592CD1	62	7494592CB1	
5202657	7	5202657CD1	63	5202657CB1	3343965CA2
2013529	8	2013529CD1	64	2013529CB1	4010537CA2, 6300041CA2
3841351	9	3841351CD1	65	3841351CB1	
152116	10	152116CD1	66	152116CB1	
2381031	11	2381031CD1	67	2381031CB1	2381031CA2
2511371	12	2511371CD1	68	2511371CB1	
8068623	13	8068623CD1	69	8068623CB1	
677977	14	677977CD1	70	677977CB1	
1661472	15	1661472CD1	71	1661472CB1	
1748508	16	1748508CD1	72	1748508CB1	90132493CA2
2159545	17	2159545CD1	73	2159545CB1	
8560269	18	8560269CD1	74	8560269CB1	
8710302	19	8710302CD1	75	8710302CB1	
6778214	20	6778214CD1	76	6778214CB1	
258383	21	258383CD1	77	258383CB1	90140053CA2, 90140161CA2
2804937	22	2804937CD1	78	2804937CB1	
7494915	23	7494915CD1	79	7494915CB1	
2073751	24	2073751CD1	80	2073751CB1	
3178841	25	3178841CD1	81	3178841CB1	
3674807	26	3674807CD1	82	3674807CB1	3674807CA2
1794922	27	1794922CD1	83	1794922CB1	90144984CA2
1795509	28	1795509CD1	84	1795509CB1	690351CA2, 90131912CA2, 90131949CA2, 90131952CA2, 90131960CA2, 90131976CA2, 90131992CA2, 90132060CA2, 90132084CA2, 90132092CA2

Table 1

Incyte Project ID	Polypeptide SEQ ID NO:	Incyte Polypeptide ID	Polynucleotide SEQ ID NO:	Incyte Polynucleotide ID	Incyte Full Length Clones
2017180	29	2017180CD1	85	2017180CB1	2807727CA2
219442	30	219442CD1	86	219442CB1	
2597459	31	2597459CD1	87	2597459CB1	90140160CA2
2783863	32	2783863CD1	88	2783863CB1	
2902971	33	2902971CD1	89	2902971CB1	
368660	34	368660CD1	90	368660CB1	90130001CA2
2804990	35	2804990CD1	91	2804990CB1	7616219CA2
168571	36	168571CD1	92	168571CB1	
1286391	37	1286391CD1	93	1286391CB1	
2007684	38	2007684CD1	94	2007684CB1	
2227040	39	2227040CD1	95	2227040CB1	
4346130	40	4346130CD1	96	4346130CB1	
55117040	41	55117040CD1	97	55117040CB1	55117036CA2
7472392	42	7472392CD1	98	7472392CB1	6622373CA2
4028960	43	4028960CD1	99	4028960CB1	
8227004	44	8227004CD1	100	8227004CB1	3279686CA2
3044763	45	3044763CD1	101	3044763CB1	90126287CA2
4044519	46	4044519CD1	102	4044519CB1	4044519CA2, 90106511CA2, 90106619CA2, 90106627CA2, 90106659CA2
71351918	47	71351918CD1	103	71351918CB1	
8109363	48	8109363CD1	104	8109363CB1	3853651CA2, 6859649CA2
1272746	49	1272746CD1	105	1272746CB1	
1839974	50	1839974CD1	106	1839974CB1	90120531CA2
1877336	51	1877336CD1	107	1877336CB1	
2321054	52	2321054CD1	108	2321054CB1	1236972CA2, 1398127CA2, 2245649CA2, 2321054CA2, 90106305CA2, 90106337CA2, 90106353CA2, 90106361CA2, 90106369CA2, 90106377CA2, 90106385CA2, 90106393CA2, 90106405CA2, 90106429CA2, 90106437CA2, 90106469CA2, 90106493CA2
2796034	53	2796034CD1	109	2796034CB1	
4413112	54	4413112CD1	110	4413112CB1	90108176CA2, 90172662CA2



Table 1

Incyte Project ID	Polypeptide SEQ ID NO:	Incyte Polypeptide ID	Polynucleotide SEQ ID NO:	Incyte Polynucleotide ID	Incyte Full Length Clones
7654832	55	7654832CD1	111	7654832CB1	90110764CA2, 90110788CA2, 90110880CA2
7503849	56	7503849CD1	112	7503849CB1	

Table 2

Polypeptide SEQ ID NO:	Incyte Polypeptide ID	GenBank ID NO: or PROTEOME ID NO:	Probability Score	Annotation
1	2867236CD1	g11065721	3.50E-134	[Homo sapiens] 28kD interferon responsive protein
4	7494391CD1	g13506808	5.70E-42	[Mus musculus] thymic stromal co-transporter
7	5202657CD1	g3006139	7.90E-42	Chen, C., et al., Biochim. Biophys. Acta 1493:159-169 (2000)
15	1661472CD1	g6899934	1.90E-24	[Schizosaccharomyces pombe] hypothetical zf-C3HC4 zinc finger protein
17	2159545CD1	g4650844	3.40E-120	[Arabidopsis thaliana] putative zinc-finger protein
18	8560269CD1	g18252514	1.00E-123	[Homo sapiens] Kelch motif containing protein
20	6778214CD1	g57671	8.90E-15	[Homo sapiens] hepatocellular carcinoma-associated antigen HCA557b
22	2804937CD1	g6650377	0	[Rattus norvegicus] ribonuclease inhibitor
23	7494915CD1	g2072953	1.60E-34	Kawanomoto, M., et al., Biochim. Biophys. Acta 1129:335-338 (1992)
24	2073751CD1	g18652658	4.00E-17	[Mus musculus] pectanex 1
31	2597459CD1	g7243777	2.90E-50	[Homo sapiens] putative p150
35	2804990CD1	g1196425	4.60E-28	Sassaman, D.M. et al. (1997) Nature Genet. 16:37-43
36	168571CD1	g3093476	6.90E-90	[Schmidtea mediterranea] myosin heavy chain A
39	2227040CD1	g1799568	1.50E-80	[Drosophila melanogaster] Diablo
40	4346130CD1	g15625572	0	[Homo sapiens] envelope protein
42	7472392CD1	g12853030	3.00E-81	Cohen, M. et al. (1985) Virology 147:449-458
43	4028960CD1	g6063688	4.50E-102	[Homo sapiens] EVI-5 homolog
44	8227004CD1	g11527201	6.70E-250	[Homo sapiens] Oncogene 14:1023-1029
				Liao, X. et al. (1997) Oncogene 14:1023-1029
				[Homo sapiens] stac
				Suzuki H., et al. (1996) Biochem. Biophys. Res. Commun. 229:902-909
				[Homo sapiens] centaurin delta1
				[Mus musculus] Cyclic nucleotide-binding domain containing protein--data source:Pfam, source key:PF00027, evidence:ISS-putative
				[Homo sapiens] AMMECR1
				Vitelli, F., et al., Genomics 55:335-340 (1999)
				[Homo sapiens] sporulation-induced transcript 4-associated protein SAPLa
				Twells, R.C.J., et al., Genomics 72:231-242 (2001)

Table 2

Polypeptide SEQ ID NO:	Incyte Polypeptide ID	GenBank ID NO: or PROTEOME ID NO:	Probability Score	Annotation
47	71351918CD1	g1314316	6.30E-73	[Xenopus laevis] WD-40 motifs; up-regulated by thyroid hormone in tadpoles Brown, D.D., et al., Proc. Natl. Acad. Sci. U.S.A. 9:1924-1929 (1996)
52	2321054CD1	g15278367	4.00E-52	[Homo sapiens] Similar to fasciculation and elongation protein zeta 2 (zygin II)
55	7654832CD1	g15420869	0	[Mus musculus] ankyrin repeat-containing SOCS box protein 5 Kile, B.T., et al., Mol. Cell. Biol. 21:6189-6197 (2001)

Table 3

SEQ ID NO:	Incyte Polypeptide ID	Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Domains and Motifs	Analytical Methods and Databases
1	2867236CD1	246	S99 S212 T11 T26 T73 T111 T131	N129 N201		
2	1294096CD1	325	S6 S25 S54 S142 S151 S162 S204 S304 S316 T47 T51 T252 T267 Y119	N254	K+ channel tetramerisation domain: D34-Q134	HMMER_PFAM
3	7238537CD1	376	S34 S52 S96 S106 S113 S118 S264 S359 S373 T38 T231 T286	N152 N319	Cytosolic domain: S321-A376 Transmembrane domain: T298-V320 Non-cytosolic domain: M1-V297	TMHMMER
4	7494391CD1	461	S48 S70 S93 S233 S253 S440 S454 S459 T166 Y39	N38 N46 N53 N143 N229 N251	Sugar transport proteins signature 1: L91-S107	MOTIFS
					Cytosolic domain: M1-V6, D96-K101, D157-R168, G219-F258, S319-D324, K374-L384, K437-R461 Transmembrane domain: E7-Y29, I78-S95, F102-F124, S134-V156, I169-I191, F196-L218, L259-F281, F296-F318, I325-T347, M351-S373, F385-Y407, F417-V436 Non-cytosolic domain: R30-D77, A125-A133, R192-G195, I282-V295, T348-M350, S408-G416	TMHMMER
5	6451054CD1	168	S26 S28 S47 S80 S85 S98 S113 T96	N50		

Table 3

SEQ ID NO:	Incyte Polypeptide ID	Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Domains and Motifs	Analytical Methods and Databases
6	7494592CD1	832	S201 S363 S470 S489 S557 S580 S658 S702 S785 S799 S818 T166 T228 T324 T352 T366 T371 T399 T545 T659 T734 Y430	N586		
7	5202657CD1	393	S28 S135 S180 S190 Y35 Y218 Y252	N189	PROTEIN C29A3.03C CHROMOSOME II ZINC FINGER NUCLEAR DNABINDING CODED FOR BY PD024560: E158-F393	BLAST_PRODOM
8	2013529CD1	280	S41 S77 S138 S144 S159 S183 S193 S235 S252 S257 S272 T20 T155 T158 T178	N232		
9	3841351CD1	344	S5 S14 S15 S33 S38 S169 T130 T173 T271 T276	N217		
10	152116CD1	405	S139 S163 S292 S322 S346 S361 T10 T70 T151 T325	N147		
11	2381031CD1	185	S52 S56 S130 S134 S143 S145 S181 T60	N121 N141		

Table 3

SEQ ID NO:	Incyte Polypeptide ID	Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Domains and Motifs	Analytical Methods and Databases
12	2511371CD1	463	S8 S261 S300 S330 T47 T88 T166 T313		Trp-Asp (WD) repeat protein BL00678: S210-W220	BLIMPS_BLOCKS
					WD domain, G-beta repeat: C186-R221, P343-D376, P254-K290	HMMER_PFAM
13	8068623CD1	403	S85 S106 S164 S389 T324 T364		TBC domain: E57-C268	HMMER_PFAM
					Cytosolic domain: R261-T364 Transmembrane domain: L238-Y260, N365-V387 Non-cytosolic domain: M1-R237, K388-P403	TMHMMER
14	677977CD1	574	S45 S57 S65 S79 S80 S218 S234 S246 S340 S376 T53 T58 T519	N214	signal_cleavage: M1-A22	SPSCAN
					Cell attachment sequence: R203-D205	MOTIFS
15	1661472CD1	731	S9 S100 S121 S156 S160 S219 S264 S339 S340 S393 S422 S450 S590 S625 S669 S672 T85 T222 T359 T377 T491 T561 T648 Y23	N335	PROTEIN ZINC FINGER CONSERVED CHROMOSOME IV COSMID CODED FOR BY C PD043678: D4-R101	BLAST_PRODOR
					PROLINE-RICH PROTEIN DM03894[P05142]1-134: V460-P550	BLAST_DOMO
					Zinc finger, C2H2 type, domain: C16-H37	MOTIFS
16	1748508CD1	299	S75 S117 S166 S206 T226	N42 N110		

Table 3

SEQ ID NO:	Incyte Polypeptide ID	Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Domains and Motifs	Analytical Methods and Databases
17	2159545CD1	620	S7 S32 S34 S127 S218 S297 S307 S354 S475 S522 S531 T70 T106 T311 T316 T390 T401 T448 T542 Y306	N29	BTB/POZ domain: K51-F164	HMIMER_PFAM
					Kelch motif: R355-N400, R496-T541, K402-N447, P449-G494, P543-S588, S307-N353	HMIMER_PFAM
					PROTEIN REPEAT MATRIX RING CANAL KELCH R12E2.1 C47D12.7 KIAA0132 KIAA0469 PD001473: P166-L294	BLAST_PRODOR
					POZ DOMAIN	BLAST_DOMO
18	8560269CD1	218	S68 S133 T55 T91 T93 T151	N28 N165	DM00509 Q04652 I31-335: E65-L238 DM00509 A45773 I30-334: E65-L238 DM00509 P21073 I-198: F60-Q243 Leucine zipper pattern: L141-L162	MOTIFS
19	8710302CD1	427	S22 S38 T118 T368 Y331		Cytosolic domain: R90-T115 Transmembrane domain: E67-L89, I116-F138 Non-cytosolic domain: M1-P66, R139-S427	TMHMMER
20	6778214CD1	612	S50 S191 S232 S359 S370 S388 S435 S473 S505 S507 S509 S511 S590 S607 T47 T72 T144 T439 T478	N70 N168 N228 N275 N360 N416		

Table 3

SEQ ID NO:	Incyte Polypeptide ID	Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Domains and Motifs	Analytical Methods and Databases
21	258383CD1	458	S22 S38 S120 T149 T399 Y362		Cytosolic domain: R90-K95, R170-Q299, S355-S458 Transmembrane domain: E67-L89, F96-L115, I147-F169, L300-R322, I332-A354 Non-cytosolic domain: M1-P66, I116-T146, N323-I331	TMHMMER
22	2804937CD1	1451	S14 S28 S168 S222 S367 S369 S483 S490 S649 S691 S768 S787 S821 S822 S884 S885 S923 S944 S968 S978 S1045 S1093 S1111 S1242 S1247 S1262 S1267 S1330 S1348 S1372 S1392 S1397 S1421 T637 T832 T977 T1438 Y446 Y562 Y635 Y845 Y1355	N201 N265 N689 N830 N1092 N1172 N1182 N1344 N1370	Cytosolic domain: M1-N116, R200-V219, G293-H303, Q399-Y404 Transmembrane domain: V117-F139, I177-S199, F220-L242, L270-Y292, I304-S323, L376-L398, V405-P422 Non-cytosolic domain: R140-I176, L243-S269, R324-D375, Q423-V1451	TMHMMER
					PROTEIN COSMID 30B8 KIAA0435 B0511.12 PECANEX DEVELOPMENTAL NEUROGENESIS TRANSMEMBRANE GLYCOPROTEIN PD014553: N636-G1198	BLAST_PRODOM



Table 3

SEQ ID NO:	Incyte Polypeptide ID	Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Domains and Motifs	Analytical Methods and Databases
22	(cont.)				PROTEIN B0511.12 COSMID 30B8 PECANEX DEVELOPMENTAL NEUROGENESIS TRANSMEMBRANE GLYCOPROTEIN REPEAT PD018553: L66-L287, S354-I471, S280-P359, G1148-N1178	BLAST_PRODOM
					PROTEIN COSMID 30B8 PECANEX DEVELOPMENTAL NEUROGENESIS TRANSMEMBRANE GLYCOPROTEIN REPEAT B0511.12 PD025614: W1379-V1444, P1179-P1207	BLAST_PRODOM
23	7494915CD1	184	S9 T24 T30 T36 T66	N22	Reverse transcriptase (RNA-dependent DNA polymerase): R86-S159	HMMER_PFAM
					Cytosolic domain: M1-L153	TMHMMER
					Transmembrane domain: F154-V176	
					Non-cytosolic domain: K177-H184	
					DNA RNADIRECTED POLYMERASE PUTATIVE P150 TRANSCRIPTASE REVERSE PROTEIN L1 SEQUENCE PD002004: Q25-L88	BLAST_PRODOM
					TRANSCRIPTASE; REVERSE; ORF2; ENCODE; DM01377 P08548 132-516: T24-M100	BLAST_DOMO
					DM01377 P08547 132-516: Q25-M100	
					DM01377 I38588 130-517: Q25-M100	
					DM01377 S16783 I-259: Q18-M100	
24	2073751CD1	407	S179 S273 S283 T61 T129 T213 T294 T306 T376 T379 T386 Y22	N247	PROTEIN COILED COIL CHAIN MYOSIN REPEAT HEAVY ATPBINDING FILAMENT HEPTAD PD000002: E128-E366 (Pvalue=2.3e-10)	BLAST_PRODOM
					Leucine zipper pattern: L301-L322	MOTIFS

Table 3

SEQ ID NO:	Incyte Polypeptide ID	Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Domains and Motifs	Analytical Methods and Databases
25	317884ICD1	261	S40 S56 S70 S140 S144 T234		HYPOTHETICAL 32.0 KD PROTEIN C09F5.2 IN CHROMOSOME III TRANSMEMBRANE PD128096: V45-V183	BLAST_PRODOM
					Cytosolic domains: 1-72, 123-155, 227-261 Transmembrane domains: 79-90, 101-122, 156-178, 204-226 Non-cytosolic domains: 91-99, 179-203	TMHMMER
26	3674807CD1	209	S197 T17 T187	N132	Signal peptide: M41-G90	SPSCAN
27	1794922CD1	333	S6 S17 S39 S65 S140 S174 S212 S241 T31 T217 T310 Y261	N63 N295		MOTIFS
28	1795509CD1	257	T43 T168 Y105		COSMID E04F6 PD132304: F72-C254 Cell attachment sequence: R78-D80	BLAST_PRODOM MOTIFS
29	2017180CD1	293	S5 S120 S135 S155 S251 S255 S279 S288 T27 T42 T107 T142	N273 N287		MOTIFS

Table 3

SEQ ID NO:	Incyte Polypeptide ID	Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Domains and Motifs	Analytical Methods and Databases
30	219442CD1	598	S28 S66 S71 S102 S149 S163 S180 S186 S191 S215 S228 S263 S283 S287 S361 S365 S406 S439 S543 S561 S571 S584 T45 T67 T172 T185 T276 T290 T337 T472 T492 T545	N195 N220 N227		MOTIFS
31	2597459CD1	470	S3 S8 S23 S78 S177 S196 S201 S359 S377 S451 T157 T279 Y101 Y292 Y309	N25 N155 N325	BTB/POZ domain: D26-L139	HMIMER_PFAM
					Kelch motif: G335-K385, C387-D433	HMIMER_PFAM
					BTB Domain PF00651: A55-F67	BLIMPS_PFAM
					PROTEIN DNA-BINDING ZINC FINGER METAL BINDING NUCLEAR ZINC FINGER TRANSCRIPTION REGULATION	BLAST_PRODOR
					CHROMOSOME PD000632: Q16-L139	
					POZ DOMAIN DM00509 Q04652 131-335: S21-N218 A45773 130-334: S21-N218 P21073 1-198: S23-E216 S59069 1-171: H24-L135	BLAST_DOMO

Table 3

SEQ ID NO:	Incye Polypeptide ID	Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Domains and Motifs	Analytical Methods and Databases
32	2783863CD1	311	S39 S101 S133 T136	N68	PROTEIN CHROMOSOME READING FRAME ORF TRANSMEMBRANE COSMID D8035.34P XV YOL002C PD005362; N68-S301  Cytosolic domains: 1-73, 129-140, 196-201, 257-275 Transmembrane domains: 74-96, 106-128, 141-163, 173-195, 202-224, 239-256, 276-298 Non-cytosolic domains: 97-105, 164-172, 225-238, 299-311	BLAST_PRODROM    TMHMMR
					MEMBRANE; YOL002C; CHROMOSOME; C30D11.11; DM02642 Q09749 49-323; T32-K302 Q09910 169-441; T32-V283 S62569 169-441; T32-V283 S61982 50-325; Y31-V283	BLAST_DOMO

Table 3

SEQ ID NO:	Incyte Polypeptide ID	Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Domains and Motifs	Analytical Methods and Databases
33	2902971CD1	894	S9 S14 S17 S75 S86 S97 S113 S114 S115 S141 S161 S169 S223 S267 S277 S293 S313 S327 S351 S372 S420 S431 S439 S454 S489 S536 S554 S580 S598 S705 S759 S792 S806 S868 T176 T278 T291 T323 T346 T409 T438 T581 T629 T635 T723 Y310	N106 N312 N596 N757	PROTEIN CHROMOSOME C30D11.09 I B0361.1 III PD033465: E673-K786	BLAST_PRODOR
					SPAC30D11.09; DM04663 Q10945 1-144: I662-K786 Q09909 388-532: M672-W796 S62567 388-532: M672-W796	BLAST_DOMO
					Cell attachment sequence: R425-D427	MOTIFS
					ATP/GTP-binding site motif A (P-loop): A622-T629	MOTIFS

Table 3

SEQ ID NO:	Incyte Polypeptide ID	Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Domains and Motifs	Analytical Methods and Databases
34	368660CD1	653	S37 S69 S79 S135 S225 S290 S303 S475 S482 S483 S512 S515 S516 S520 S582 S645 T373 T384 T414 T448 T453 T476 T601 T629	N288 N508 N542	TPR Domain: V341-H374, A307-N340, C382-F415	HMMER PFAM
35	2804990CD1	144	T16	N17	Cell attachment sequence: R125-D127 Cytosolic domain: 137-144 Transmembrane domain: 114-136 Non-cytosolic domain: 1-113	MOTIFS TMHMMR
36	168571CD1	424	S88 S123 S124 S151 S179 S194 S258 S269 S364 S365 S386 S407 S409 T92	N122 N311	signal_cleavage: M1-L24	SPSCAN
					EV15 HOMOLOG TRUNCATED EV15 ECOTROPIC VIRAL INTEGRATION SITE COSMID F01G12 PD075221: E84-P180 Protein kinases ATP-binding region signature: L370-K401	BLAST_PRODOM MOTIFS

Table 3

SEQ ID NO:	Incyte Polypeptide ID	Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Domains and Motifs	Analytical Methods and Databases
37	128639ICD1	1351	S187 S266 S311 S320 S359 S360 S423 S486 S496 S556 S633 S657 S704 S884 S1000 S1204 S1262 S1274 S1296 S1345 T25 T74 T95 T124 T159 T230 T329 T392 T463 T642 T691 T940 T1015 T1079 T1215	N215 N235 N358 N543 N1293	Integrase core domain: R1062-L1130	HMMER_PFAM
					POL POL YPROTEIN DM00159 S08405 760-943: H1009-A1139 DM00140 S52564 1-364: Y517-K670 Leucine zipper pattern: L837-L858	BLAST_DOMO
38	2007684CD1	78				MOTIFS
39	2227040CD1	411	S5 S39 S56 S84 S112 S122 S168 S198 S224 S232 S234 S246 S249 S325 S372 S396 T82 T188 T207 T286	N172 N218	Phorbol esters/diacylglycerol binding domain: H111-C161	HMMER_PFAM
					SH3 domain: Y295-V349 Phorbol esters / diacylglycerol binding domain proteins BL00479: H111-G133, Q137-C152	HMMER_PFAM BLIMPS_BLOCKS

Table 3

SEQ ID NO:	Incyte Polypeptide ID	Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Domains and Motifs	Analytical Methods and Databases
39					Phorbol esters / diacylglycerol binding domain: R120-S213	PROFILESCAN
(cont.)					Diacylglycerol/phorbol-ester binding signature PR00008: H158-R170, V108-S122, C124-G133, Q137-V148	BLIMPS_PRINTS
					STAC	BLAST_PRODUM
					PD027304: Q347-I411	
					PD032205: G163-G245	
					SRC HOMOLOG 3 (SH3) DOMAIN	BLAST_DOMO
					DM00025[S61138]55-108: Y297-Q347	
					Cytochrome c family heme-binding site signature: C124-Q129	MOTIFS
					Phorbol esters / diacylglycerol binding domain: H111-C161	MOTIFS



Table 3

SEQ ID NO:	Incyte Polypeptide ID	Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Domains and Motifs	Analytical Methods and Databases
40	4346130CD1	1704	S3 S165 S295 S323 S346 S350 S378 S416 S424 S480 S677 S683 S696 S699 S739 S781 S834 S911 S932 S977 S1124 S1165 S1172 S1194 S1211 S1404 S1428 S1435 S1476 S1477 S1487 S1510 S1582 S1593 S1604 T34 T83 T122 T155 T183 T190 T196 T312 T314 T357 T409 T411 T417 T437 T534 T548 T643 T663 T681 T791 T808 T919 T1011 T1096 T1105 T1215 T1279 T1369 T1423 T1524 T1639 T1656	N42 N167 N205 N231 N327 N694 N697 N943 N1009 N1572	Putative GTP-ase activating protein for Arf: Y685-L807	HMMER_PFAM
					PH domain: S1435-H1537, K483-K574, P588-A679, I879-V1003	HMMER_PFAM
					RhoGAP domain: P1129-E1282	HMMER_PFAM

Table 3

SEQ ID NO:	Incyte Polypeptide ID	Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Domains and Motifs	Analytical Methods and Databases
40					SAM domain (Sterile alpha motif): V4-L68	HMME PFAM
(cont.)					HIV Rev interacting protein signature PR00405: N697-C716, C716-K733, V484-V505	BLIMPS PRINTS
					PROTEIN GTPASE DOMAIN AC PD00930: P1129-G1154, L1232-L1272	BLIMPS_PRODROM
					PROTEIN ZINC FINGER NUCLEAR DNA BINDING PUTATIVE GTPASE ACTIVATING FACTOR CHROMOSOME REPEAT PD002425: N694-E775	BLAST_PRODROM
					PROTEIN GTPASE DOMAIN SH2 ACTIVATION ZINC 3 KINASE SH3 PHOSPHATIDYLINOSITOL REGULATORY PD000780: V1128-E1282	BLAST_PRODROM
					PH DOMAIN DM00470 [S54307 1621-1845: K1125-E1301 [P34588 1-285: K1125-N1291 [A49307 566-842: T1096-Q1274 [P15882 109-331: I1107-T1275	BLAST_DOMO
41	55117040CD1	243	S13 S38 S53 S59 S75 T45 T171	N50 N203	Ankyrin repeat: Q135-N167, K168-E200, Y201-Q230	HMME PFAM
					Aldehyde ferredoxin oxid PF01314: A110-V122, R73-L103, A82-K114	BLIMPS PFAM
42	7472392CD1	248	S7 S57 S112 S137 S157 S175 S200 T12 T180			
43	4028960CD1	310	S59 S277 S283 T98 T141 T144 T184 T199 T269	N36 N63 N93 N97 N297		

Table 3

SEQ ID NO:	Incyte Polypeptide ID	Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Domains and Motifs	Analytical Methods and Databases
44	8227004CD1	838	S11 S133 S202 S214 S304 S315 S402 S417 S503 S582 S599 S604 S616 S673 S687 S696 S700 S705 S742 S817 T15 T23 T171 T233 T274 T278 T282 T390 T411 T413 T472 T507 T512 T608 T614 T711 T751 T789	N79 N210 N231 N261 N302 N358 N409 N542 N552 N558 N647	PROTEIN SIT4-ASSOCIATING PHOSPHORYLATION CELL CYCLE SAPI55 KIAA0685 SAPI85 SAPI90 SAP4 PD014556: D68-E284	BLAST_PRODOM
					SIT4-ASSOCIATING PROTEIN SAPI90 DM03002 P40856 222-821: M92-N363	BLAST_DOMO
					SIT4-ASSOCIATING PROTEIN SAPI85 DM03002 P36123 229-825: E98-N363	BLAST_DOMO
45	3044763CD1	408	S25 S62 S68 S103 S184 S286 S330 S344 S377 S392 T98 T131 T158 T213	N257 N342	Leucine zipper pattern: L261-L282	MOTIFS
					Cytosolic domains: M1-G229, R290-R301, S377-S408 Transmembrane domains: L230-G252, T267-D289, N302-L324, I354-L376 Non-cytosolic domains: D253-K266, S325-Q353	TMHMMER
46	4044519CD1	I01	T89		Signal_cleavage: M1-S15	SPSCAN
					Signal Peptide: M1-S19, M1-T16, M31-S59	HMMER

Table 3

SEQ ID NO:	Incyte Polypeptide ID	Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Domains and Motifs	Analytical Methods and Databases
46						
(cont.)						
47	71351918CD1	256	S26 S107 S174 S194 S202 T35 T63 T222		Cytosolic domains: M1-M31, E82-L101 Transmembrane domains: V32-L54; L64-L81 Non-cytosolic domain: N55-S63 WD domain, G-beta repeat: C32-D68, Q136-D171, V179-Q212	TMHMMER HMMER_PFAM
					Non-cytosolic domain: M1-L256	TMHMMER
					Trp-Asp (WD-40) repeats signature: L44-A92	PROFILES SCAN
					Trp-Asp containing, G-protein WD-40 repeats GENE 16 PD106308: R71-L256	BLAST_PROD OM
					Trp-Asp (WD) repeats signature: V55-C69	MOTIFS
48	8109363CD1	104			Non-cytosolic domain: M1-G104	TMHMMER
49	1272746CD1	855	S27 S93 S159 S184 S245 S287 S329 S593 S708 S726 S793 S811 S827 T18 T26 T35 T45 T128 T200 T202 T319 T352 T438 T470 T601 T642 T807	N132 N157 N254 N312 N325 N486 N592 N615 N623 N659 N822	Non-cytosolic domain: M1-S855	TMHMMER
50	1839974CD1	427	S254 S277 S321 S334 S361 S365 T50 T182 T247 Y329	N73 N258 N405	Fibronectin type III domain: L276-G364	HMMER_PFAM
					Non-cytosolic domain: M1-I427	TMHMMER
					Fibronectin type III repeat signature PR00014: S393-P402, G406-W416	BLIMPS_PRINTS

Table 3

SEQ ID NO:	Incyte Polypeptide ID	Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Domains and Motifs	Analytical Methods and Databases
51	1877336CD1	800	S58 S74 S252 S277 S283 S306 S351 S380 S415 S424 S437 S439 S446 S491 S521 S534 S539 S605 S786 T208 T302 T313 T488 T553 T572 T747 T781 Y331	N272 N281 N411 N785	Non-cytosolic domain: M1-F800	TMHMMER
					FIBRILLAR COLLAGEN CARBOXYL- TERMINAL DM00019 S42886 221-377: G112-N237	BLAST_DOMO
52	2321054CD1	107	S87 T17 T62		Signal_cleavage: M1-A43 Non-cytosolic domain: M1-E24 Transmembrane domain: A25-A43 Cytosolic domain: K44-E107	SPSCAN TMHMMER
53	2796034CD1	522	S10 S49 S77 S191 S195 S204 S212 S335 S339 S344 S361 S371 S397 S443 S453 T72 T125 T138 T146 T228 T241 T245 T267 T318 T363 T496	N59 N85 N120 N487 N494	Non-cytosolic domain: M1-Q522	TMHMMER
54	4413112CD1	305	S28 S57 S98 S122 S238 S294	N44 N55 N130 N148	Signal_cleavage: M1-S20	SPSCAN
					Signal Peptide: M1-S20	HMMER

Table 3

SEQ ID NO:	Incyte Polypeptide ID	Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Domains and Motifs	Analytical Methods and Databases
54					Non-cytosolic domain: M1-T165 Transmembrane domain: I166-W188 Cytosolic domain: R189-H305	TMHMMER
					Leucine-rich repeat signature PR00019: L84-L97, V63-L76	BLIMPS_PRINTS
55	7654832CD1	329	S2 S67 S150 S244 S277 T121		Signal_cleavage: M1-G46	SPSCAN
					Cytosolic domain: M1-T20 Transmembrane domain: I21-I43 Non-cytosolic domain: V44-R329	TMHMMER
					Ank repeat: Y232-T264, D102-I134, A69-L101, D135-C167, S170-P199, H200-K231	HMMER_PFAM
56	7503849CD1	236	S34 S52 S96 S106 S113 S118 T38 T231	N152	Signal peptide: M18-A80	SPSCAN

Table 4

Polynucleotide SEQ ID NO./ Incye ID/ Sequence Length	Sequence Fragments
57/2867236CB1/ 1485	1-222, 1-461, 1-464, 1-572, 4-516, 7-279, 12-266, 16-285, 23-278, 24-281, 24-522, 30-320, 31-309, 31-316, 34-172, 34-327, 34-639, 42-282, 46-218, 46-335, 51-290, 51-342, 141-404, 141-405, 143-579, 182-471, 208-654, 208-684, 211-695, 217-453, 321-836, 335-910, 381-933, 390-996, 475-747, 475-762, 482-1009, 537-1153, 591-970, 717-993, 796-1090, 797-1382, 808-1485, 963-1280
58/1294096CB1/ 6176	1-210, 1-383, 1-416, 1-508, 1-516, 1-6176, 33-443, 33-570, 228-695, 228-1034, 365-486, 495-1170, 511-962, 574-961, 647-975, 794-1062, 959-1554, 1000-1160, 1009-1246, 1009-1497, 1034-1327, 1075-1207, 1111-1292, 1170-1258, 1250-1842, 1260-1540, 1261-1835, 1288-1927, 1292-1877, 1352-1518, 1417-1679, 1438-2085, 1446-1787, 1542-1841, 1697-1891, 1860-2146, 1872-1935, 1971-2491, 2021-2670, 2028-2623, 2108-2393, 2173-2698, 2174-2729, 2179-2427, 2192-2528, 2194-2469, 2196-2775, 2198-2432, 2205-2471, 2206-2456, 2208-2458, 2211-2451, 2212-2465, 2226-2443, 2230-2787, 2242-2498, 2270-2481, 2281-2922, 2296-2933, 2310-2564, 2320-2575, 2327-2614, 2329-2701, 2337-2663, 2350-2472, 2384-2671, 2384-3130, 2397-2558, 2397-2976, 2418-2677, 2450-2878, 2455-2608, 2470-2665, 2479-2725, 2480-2676, 2484-2768, 2496-3042, 2506-2905, 2509-2739, 2509-3040, 2512-2772, 2563-3211, 2603-2902, 2665-2928, 2667-3092, 2673-3232, 2706-3159, 2711-3168, 2719-2972, 2726-3166, 2729-2927, 2738-3165, 2743-2840, 2744-3166, 2750-2997, 2763-3037, 2779-3309, 2780-3064, 2797-3413, 2822-3091, 2829-3021, 2836-3285, 2843-3169, 2848-3438, 2852-3032, 2852-3209, 2856-3109, 2861-3546, 2881-3106, 2881-3375, 2890-3411, 2907-3364, 2910-3158, 2964-3435, 2993-3483, 2993-3597, 3009-3277, 3051-3494, 3056-3286, 3069-3279, 3069-3583, 3071-3355, 3071-3660, 3098-3530, 3103-3348, 3126-3582, 3134-3337, 3140-3709, 3145-3396, 3174-3319, 3199-3388, 3199-3854, 3201-3770, 3204-3779, 3222-3627, 3250-3667, 3284-3920, 3308-3625, 3336-3570, 3336-3594, 3336-3598, 3336-3601, 3336-3615, 3336-3617, 3336-3629, 3336-3631, 3336-3636, 3336-3669, 3342-3867, 3342-3957, 3342-3961, 3361-3965, 3370-3645, 3381-3575, 3381-3580, 3420-3832, 3435-4105, 3460-3723, 3513-4121, 3519-3784, 3521-3985, 3542-3680, 3544-3775, 3559-4065, 3569-4170, 3576-3824, 3601-3810, 3625-3753, 3633-3852, 3639-4169, 3644-3940, 3651-4246, 3673-4260, 3682-3853, 3716-4031, 3720-4094, 3720-4186, 3720-4194, 3721-4281, 3728-4206, 3728-4340, 3728-4427, 3749-4132, 3750-4001, 3750-4297, 3751-3880, 3759-4040, 3768-4266, 3778-4243, 3781-4065, 3783-4453, 3789-4049, 3796-4095, 3803-4392, 3820-4049, 3820-4052, 3820-4106, 3835-4309, 3841-4163, 3841-4185, 3852-4098, 3853-4437, 3865-4082, 3865-4389, 3868-4165, 3892-4082, 3898-4136, 3899-4211, 3937-4467, 3940-4545, 3945-4098, 3954-4496, 3963-4183,

Table 4

Polynucleotide SEQ ID NO./ Incyte ID/ Sequence Length	Sequence Fragments
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Table 4

Polynucleotide SEQ ID NO./ Incyte ID/ Sequence Length	Sequence Fragments
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Table 4

Polynucleotide SEQ ID NO./ Incyte ID/ Sequence Length	Sequence Fragments
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Table 4

Polynucleotide SEQ ID NO./ Incye ID/ Sequence Length	Sequence Fragments
61/6451054CB1/ 3906	<p>1-24, 1-27, 1-36, 1-41, 1-42, 1-43, 1-53, 1-55, 1-64, 1-65, 1-71, 1-72, 1-75, 1-80, 1-83, 1-86, 1-88, 1-89, 1-90, 1-92, 1-94, 1-95, 1-109, 1-117, 1-123, 1-130, 1-131, 1-139, 1-140, 1-170, 1-172, 1-186, 1-189, 1-190, 1-191, 1-193, 1-399, 5-189, 6-186, 7-189, 10-159, 14-151, 22-193, 29-193, 38-192, 38-193, 41-112, 44-189, 59-90, 71-193, 78-193, 79-193, 86-193, 87-193, 91-192, 96-192, 122-193, 126-193, 127-193, 133-186, 139-192, 151-192, 153-191, 158-193, 162-193, 192-680, 192-728, 433-998, 433-1007, 433-1039, 433-1040, 444-668, 453-1350, 503-782, 573-1070, 573-1166, 573-3748, 633-984, 633-1139, 639-1306, 666-1172, 683-950, 684-1132, 703-1346, 755-1518, 790-1294, 814-1423, 867-1641, 869-1468, 909-1501, 996-1644, 1009-1598, 1025-1654, 1090-1117, 1103-1320, 1103-1610, 1105-1535, 1105-1550, 1131-1438, 1136-1465, 1153-1704, 1158-1465, 1177-1419, 1178-1253, 1198-1709, 1201-1552, 1210-1552, 1224-1839, 1227-1486, 1239-1540, 1240-1540, 1249-1788, 1269-1821, 1292-1804, 1317-1499, 1332-1556, 1426-2015, 1465-1953, 1471-1707, 1487-1693, 1509-2141, 1519-1798, 1520-1609, 1570-1912, 1593-2047, 1621-1891, 1631-2218, 1723-1882, 1726-2213, 1762-2341, 1764-2348, 1764-2431, 1765-2431, 1785-2431,</p> <p>1816-2078, 1822-2074, 1843-2044, 1861-2292, 1874-2214, 1891-2776, 1921-2298, 1943-2431, 1969-2494, 1990-2610, 2003-2306, 2011-2255, 2029-2290, 2029-2442, 2078-2299, 2079-2599, 2094-2558, 2121-2320, 2121-2323, 2127-2428, 2128-2336, 2128-2623, 2129-2857, 2136-2731, 2140-2430, 2155-2620, 2191-2846, 2198-2731, 2200-2731, 2206-2460, 2210-2444, 2211-2367, 2217-3127, 2227-2447, 2243-2806, 2320-2898, 2325-2981, 2340-2767, 2354-2493, 2356-2466, 2358-2592, 2358-2740, 2373-2485, 2374-2561, 2374-2857, 2374-2892, 2378-2661, 2380-2652, 2383-2656, 2394-2976, 2396-3005, 2430-3135, 2447-2699, 2447-2706, 2470-3044, 2473-2759, 2474-3022, 2482-3005, 2492-3007, 2498-2986, 2502-2946, 2503-2634, 2510-2706, 2510-3005, 2515-2964, 2516-2747, 2522-3007, 2524-2768, 2527-2656, 2535-3028, 2555-2858, 2555-3132, 2555-3133, 2556-2825, 2559-2819, 2573-2795, 2593-2863, 2595-2857, 2598-2836, 2603-2876, 2603-2926, 2617-3043, 2619-2887, 2620-3067, 2623-2761, 2635-3021, 2646-2908, 2649-3215, 2651-3260, 2652-3135, 2653-3065, 2659-3420, 2665-2946, 2679-3186, 2683-3348, 2684-3235, 2686-3166, 2687-3162, 2689-3174, 2711-2945, 2716-2983, 2732-2988, 2737-3247, 2739-3202,</p>

Table 4

Polynucleotide SEQ ID NO./ Incyte ID/ Sequence Length	Sequence Fragments
61 (cont.)	2776-3348, 2783-3290, 2789-3052, 2790-3247, 2796-3045, 2799-3054, 2802-3423, 2830-3094, 2834-3460, 2846-3098, 2847-3046, 2862-3145, 2866-3107, 2867-3029, 2869-3162, 2871-3253, 2871-3410, 2875-3131, 2891-3193, 2893-3193, 2900-3149, 2900-3494, 2901-3485, 2914-3137, 2922-3185, 2922-3381, 2925-3444, 2927-3495, 2932-3584, 2947-3420, 2957-3233, 2959-3210, 2966-2998, 2991-3259, 2994-3597, 2997-3580, 3004-3264, 3013-3571, 3016-3181, 3023-3228, 3025-3299, 3025-3348, 3025-3662, 3026-3224, 3046-3308, 3051-3315, 3053-3526, 3057-3562, 3059-3739, 3063-3300, 3079-3640, 3081-3742, 3096-3564, 3104-3748, 3105-3738, 3116-3737, 3119-3680, 3121-3358, 3127-3307, 3127-3647, 3128-3432, 3128-3701, 3129-3295, 3133-3513, 3145-3733, 3146-3739, 3156-3365, 3156-3417, 3156-3427, 3156-3616, 3156-3738, 3175-3733, 3184-3635, 3188-3418, 3190-3742, 3193-3386, 3200-3407, 3200-3697, 3214-3457, 3214-3742, 3216-3738, 3227-3676, 3235-3691, 3246-3742, 3246-3743, 3247-3746, 3255-3531, 3255-3748, 3256-3742, 3263-3491, 3263-3751, 3269-3536, 3274-3345, 3277-3396, 3277-3549, 3291-3748, 3292-3742, 3294-3748, 3296-3327, 3296-3703, 3296-3760, 3297-3742, 3298-3748, 3300-3548, 3300-3559, 3300-3743, 3300-3748, 3303-3748, 3306-3746, 3311-3748, 3314-3748, 3315-3748, 3321-3756, 3322-3755, 3322-3760, 3331-3754, 3333-3760, 3342-3749, 3343-3746, 3344-3747, 3345-3616, 3346-3742, 3351-3750, 3360-3746, 3363-3748, 3371-3713, 3371-3748, 3372-3524, 3375-3741, 3377-3746, 3378-3748, 3382-3740, 3389-3748, 3395-3674, 3397-3742, 3409-3664, 3410-3746, 3413-3746, 3417-3688, 3419-3711, 3423-3746, 3428-3760, 3440-3746, 3443-3748, 3450-3746, 3450-3748, 3455-3746, 3461-3732, 3469-3760, 3480-3681, 3482-3543, 3496-3735, 3496-3748, 3499-3732, 3504-3733, 3504-3735, 3504-3747, 3504-3760, 3519-3742, 3528-3748, 3535-3748, 3585-3748, 3603-3735, 3609-3748, 3612-3748, 3614-3906, 3636-3748, 3665-3739
62/494592CB1/ 3236	1-234, 8-614, 30-557, 30-619, 31-226, 102-429, 127-689, 134-799, 150-400, 186-834, 238-571, 520-1276, 624-1216, 688-1195, 721-851, 792-1518, 821-1162, 835-1154, 905-1626, 916-1626, 922-1626, 943-1222, 953-1499, 1086-1616, 1112-1702, 1246-1665, 1251-1676, 1313-1858, 1441-1854, 1465-1919, 1477-1620, 1642-2180, 1697-1860, 1716-2387, 1778-2128, 1796-2083, 1822-2371, 1846-2158, 1905-2422, 1973-2308, 2075-2187, 2092-2626, 2092-2631, 2094-2362, 2101-2662, 2191-2810, 2243-2655, 2506-2824, 2570-3236, 2572-2827

Table 4

Polynucleotide SEQ ID NO./ Incyte ID/ Sequence Length	Sequence Fragments
63/5202657CB1/ 1906	1-237, 1-525, 2-270, 3-277, 3-300, 3-557, 3-567, 7-270, 7-275, 8-292, 8-529, 12-207, 12-248, 12-606, 26-274, 26-541, 27-276, 28-572, 29-306, 33-244, 33-330, 76-714, 119-450, 119-451, 125-371, 272-537, 296-556, 324-467, 553-990, 555-813, 555-961, 557-812, 557-814, 571-812, 605-799, 608-860, 656-884, 661-927, 669-931, 712-959, 712-976, 712-992, 713-980, 716-1007, 777-1048, 798-1050, 884-1405, 890-1120, 902-1175, 929-1294, 998-1533, 1018-1432, 1037-1198, 1055-1230, 1061-1563, 1062-1283, 1064-1326, 1066-1342, 1068-1333, 1075-1396, 1079-1305, 1085-1345, 1085-1370, 1094-1347, 1102-1313, 1102-1321, 1102-1658, 1102-1789, 1139-1396, 1151-1648, 1177-1403, 1183-1867, 1198-1894, 1205-1491, 1210-1827, 1226-1563, 1230-1834, 1237-1663, 1259-1874, 1264-1838, 1265-1544, 1268-1882, 1275-1566, 1284-1586, 1296-1516, 1303-1496, 1344-1583, 1346-1906, 1353-1874, 1359-1594, 1366-1748, 1373-1635, 1375-1656, 1375-1851, 1378-1618, 1378-1619, 1393-1594, 1393-1631, 1393-1656, 1398-1751, 1425-1894, 1441-1898, 1446-1872, 1450-1906, 1455-1855, 1459-1891, 1462-1718, 1462-1878, 1467-1864, 1475-1898, 1520-1793, 1520-1890, 1529-1878, 1536-1760, 1536-1823, 1558-1891, 1560-1890, 1587-1792, 1602-1870, 1606-1851, 1622-1872, 1636-1906, 1697-1906, 1708-1886, 1755-1891, 1776-1874
64/2013529CB1/ 1347	1-153, 1-293, 1-303, 1-322, 1-383, 1-423, 1-469, 1-478, 1-483, 1-484, 1-490, 1-507, 1-560, 1-603, 1-611, 1-627, 1-654, 1-659, 1-660, 2-554, 2-630, 15-313, 15-636, 25-303, 25-328, 48-793, 64-554, 108-793, 183-441, 254-777, 279-567, 282-556, 331-616, 341-1071, 350-604, 350-889, 374-591, 374-665, 413-610, 415-683, 455-1085, 517-848, 517-924, 518-1149, 529-1098, 573-1203, 618-998, 634-1303, 647-1224, 675-1318, 681-895, 681-1040, 681-1057, 681-1077, 681-1090, 681-1091, 681-1094, 681-1199, 681-1201, 681-1205, 681-1215, 681-1223, 681-1303, 681-1312, 684-1127, 684-1308, 751-1347, 761-1347, 771-1347, 816-1312, 908-1312, 916-1334, 929-1310, 1062-1347, 1089-1310, 1128-1312, 1172-1310
65/3841351CB1/ 1854	1-585, 1-1854, 21-594, 29-721, 31-630, 34-302, 46-582, 49-289, 74-312, 474-875, 632-884, 632-1014, 632-1230, 632-1287, 675-1276, 761-1254, 814-1392, 850-1273, 864-1103, 904-1208, 906-1431, 945-1276, 949-1268, 1207-1854, 1208-1608, 1316-1854, 1378-1603, 1410-1800, 1473-1560
66/152116CB1/ 1327	1-568, 74-694, 81-697, 93-579, 105-775, 108-291, 239-902, 468-718, 468-869, 515-761, 579-838, 583-1327, 670-1289, 685-1291, 700-896, 872-1287

Table 4

Polynucleotide SEQ ID NO./ Incyte ID/ Sequence Length	Sequence Fragments
67/2381031CBI/ 627	1-225, 1-515, 1-604, 2-254, 3-272, 7-185, 7-266, 7-286, 7-290, 7-291, 7-294, 7-296, 8-207, 9-301, 11-307, 11-319, 15-264, 16-250, 17-278, 17-290, 17-295, 17-572, 18-246, 20-373, 22-301, 29-271, 29-287, 32-202, 32-257, 32-273, 32-291, 32-338, 32-343, 35-293, 35-295, 35-348, 37-194, 37-397, 37-452, 43-360, 51-327, 154-435, 155-617, 156-433, 157-627, 158-607, 158-612, 162-378, 162-379, 164-615, 168-479, 169-627, 185-627, 188-606, 189-627, 204-609, 223-607, 233-409, 254-615, 284-556, 292-573, 300-606, 344-529, 366-612, 418-627
68/2511371CBI/ 2564	1-577, 237-1628, 328-691, 328-892, 334-925, 373-975, 496-1062, 557-1106, 686-855, 921-978, 1002-1634, 1053-1594, 1091-1766, 1102-1630, 1209-1827, 1210-1767, 1213-1642, 1213-1926, 1286-1943, 1305-1700, 1316-1945, 1336-1800, 1341-1981, 1341-2008, 1344-1908, 1345-1935, 1349-1899, 1464-2013, 1492-2061, 1503-1967, 1569-2167, 1581-2170, 1662-2343, 1695-2351, 1746-2337, 1746-2400, 1750-2394, 1756-2418, 1772-2316, 1776-2497, 1902-2429, 1924-2453, 1930-2564
69/8068623CBI/ 4134	1-1457, 1292-1820, 1292-1831, 1292-1843, 1292-1908, 1292-1933, 1305-2006, 1306-1967, 1307-1900, 1307-1942, 1313-1790, 1319-1826, 1320-2234, 1322-1920, 1327-1889, 1331-1976, 1332-1610, 1352-1908, 1399-1856, 1439-1929, 1485-1694, 1485-2040, 1501-1939, 1510-2089, 1516-2152, 1516-2156, 1516-2175, 1616-1985, 1695-1933, 1695-1942, 1738-1934, 1810-2017, 1810-2271, 1862-2339, 1882-2248, 1941-2478, 1961-2212, 1961-2214, 1970-2218, 1975-2115, 1989-2719, 2009-2287, 2019-2457, 2019-2568, 2029-2269, 2046-2627, 2051-2697, 2055-2587, 2167-2434, 2185-2435, 2213-2829, 2258-2521, 2336-2525, 2408-2941, 2409-2620, 2430-2714, 2478-3024, 2547-3147, 2670-2933, 2674-2921, 2674-3216, 2788-3037, 2867-3224, 2867-3445, 2908-3173, 2959-3159, 2959-3186, 2998-3252, 2998-3544, 3104-3358, 3195-3383, 3195-3432, 3285-3557, 3310-3502, 3368-3647, 3387-3642, 3410-3598, 3491-3643, 3491-4021, 3499-3753, 3554-4134, 3610-3749, 3629-3859, 3652-3900, 3776-4011
70/677977CBI/ 2329	1-1548, 464-1093, 467-1093, 482-1093, 496-1093, 502-1093, 504-1093, 506-1093, 513-1093, 515-1093, 528-1093, 529-1093, 569-1093, 588-1093, 612-1088, 626-1093, 627-1093, 655-976, 678-1093, 694-1093, 903-1166, 927-1448, 1119-1860, 1161-1830, 1211-1741, 1253-1481, 1374-2024, 1378-1640, 1414-1546, 1414-1548, 1439-1704, 1461-2042, 1467-1985, 1482-1548, 1512-1548, 1516-1548, 1519-1548, 1522-1548, 1548-1636, 1548-1733, 1548-1740, 1548-1763, 1548-1764, 1548-1788, 1548-2001, 1548-2080, 1548-2147, 1548-2195, 1548-2210, 1548-2220, 1548-2329, 1578-1656, 1582-1851, 1585-2146, 1588-1849, 1588-2097

Table 4

Polynucleotide SEQ ID NO./ Incyte ID/ Sequence Length	Sequence Fragments
71/1661472CB1/ 2960	1-389, 2-389, 4-26, 18-2925, 96-815, 118-777, 333-923, 366-622, 369-907, 482-1135, 536-1004, 573-812, 661-1021, 739-973, 739-1245, 743-1323, 774-1466, 793-1368, 882-1005, 927-1440, 964-1514, 1008-1582, 1035-1321, 1291-1719, 1305-1567, 1305-1721, 1369-1547, 1419-1666, 1419-1795, 1630-1685, 1675-2070, 1766-2529, 1781-2148, 1781-2152, 1781-2164, 1781-2210, 1781-2221, 1781-2275, 1781-2292, 1781-2457, 1782-2446, 1799-2194, 1812-2291, 1839-2037, 1839-2318, 1843-2466, 1883-2459, 1893-2298, 1904-2271, 1935-2144, 1935-2150, 1939-2197, 1941-2200, 1941-2541, 1942-2327, 1949-2152, 1949-2206, 1994-2214, 1996-2151, 1997-2253, 2004-2298, 2005-2756, 2010-2248, 2028-2282, 2032-2262, 2032-2283, 2038-2258, 2038-2372, 2038-2489, 2039-2723, 2046-2331, 2053-2544, 2055-2802, 2102-2744, 2111-2313, 2127-2345, 2127-2622, 2132-2914, 2140-2373, 2160-2754, 2161-2417, 2164-2392, 2166-2412, 2176-2445, 2203-2384, 2233-2883, 2239-2536, 2239-2548, 2259-2497, 2270-2541, 2272-2520, 2285-2451, 2285-2761, 2306-2855, 2328-2760, 2341-2592, 2349-2619, 2349-2796, 2357-2810, 2372-2948, 2377-2628, 2385-2811, 2391-2811, 2403-2893, 2439-2857, 2443-2920, 2453-2926, 2468-2925, 2478-2921, 2483-2922, 2488-2960, 2497-2938, 2499-2923, 2500-2917, 2502-2920, 2504-2948, 2511-2923, 2515-2923, 2520-2928, 2543-2926, 2549-2700, 2557-2920, 2568-2923, 2584-2934, 2595-2924, 2597-2914, 2726-2920, 2770-2924, 2773-2924
72/1748508CB1/ 2623	1-523, 57-749, 89-761, 392-889, 473-739, 545-1327, 592-1314, 640-1337, 678-1404, 706-1471, 741-868, 860-1366, 896-1143, 912-1385, 916-1156, 920-1172, 981-1578, 1067-1925, 1097-1796, 1150-1427, 1182-1797, 1240-1957, 1299-1529, 1322-1592, 1322-1603, 1322-1617, 1322-1737, 1322-1931, 1322-1962, 1345-1623, 1348-1770, 1352-1619, 1353-1624, 1384-1750, 1384-1997, 1392-1661, 1439-1709, 1558-1769, 1558-1938, 1614-1899, 1725-2254, 1801-2046, 1859-2113, 1951-2195, 1951-2505, 1951-2603, 1953-2098, 1954-2495, 1956-2480, 1959-2116, 1963-2501, 1963-2511, 1967-2209, 1980-2512, 1988-2601, 2010-2582, 2010-2613, 2046-2595, 2063-2584, 2064-2588, 2079-2616, 2085-2358, 2092-2257, 2098-2617, 2103-2502, 2106-2616, 2114-2616, 2122-2407, 2128-2592, 2138-2592, 2141-2598, 2142-2595, 2142-2598, 2147-2599, 2148-2614, 2166-2616, 2167-2599, 2175-2307, 2182-2595, 2200-2595, 2201-2623, 2202-2595, 2207-2592, 2226-2597, 2229-2595, 2235-2505, 2244-2595, 2246-2616, 2263-2595, 2264-2542, 2269-2565, 2288-2595, 2288-2597, 2297-2592, 2324-2578, 2344-2595, 2372-2615, 2424-2615, 2535-2599

Table 4

Polynucleotide SEQ ID NO:/ Incyte ID/ Sequence Length	Sequence Fragments
73/2159545CB1/ 4518	1-625, 1-695, 9-773, 46-2189, 275-1051, 343-822, 704-4518, 987-1569, 990-1563, 992-1230, 992-1443, 1029-1388, 1260-1989, 1262-1572, 1263-1572, 1266-1569, 1266-1572, 1314-1570, 1363-1613, 1363-1912, 1520-2058, 1588-2056, 1588-2086, 1590-1883, 1660-2224, 1736-2117, 1747-1939, 1781-2041, 1781-2324, 1798-2058, 1912-2216
74/8560269CB1/ 1238	1-263, 1-272, 1-329, 65-281, 65-332, 67-209, 90-274, 90-389, 91-270, 132-788, 331-583, 346-802, 348-620, 358-949, 509-1075, 559-1024, 619-1030, 620-826, 620-879, 620-1031, 666-875, 666-1129, 678-1093, 736-1091, 764-1057, 783-1107, 785-1045, 785-1078, 785-1088, 918-1184, 1020-1238
75/8710302CB1/ 1771	1-226, 82-368, 96-381, 125-423, 180-915, 184-395, 188-437, 189-379, 481-984, 493-989, 499-917, 500-980, 550-869, 558-991, 561-973, 561-991, 563-991, 565-1159, 569-1250, 606-1103, 667-1226, 688-1356, 714-974, 714-1216, 718-989, 771-1028, 844-1142, 846-1402, 914-1493, 943-1371, 1032-1571, 1041-1598, 1041-1623, 1091-1369, 1091-1372, 1091-1700, 1110-1383, 1154-1723, 1158-1444, 1273-1771, 1327-1598, 1330-1616
76/6778214CB1/ 2909	1-143, 60-830, 148-772, 165-441, 182-425, 207-373, 217-893, 342-479, 381-851, 400-885, 404-851, 407-764, 415-886, 420-851, 431-851, 432-867, 438-1047, 455-851, 475-882, 501-851, 515-851, 541-851, 550-813, 551-859, 568-851, 580-844, 621-880, 694-875, 871-1537, 882-1105, 883-1469, 884-1313, 888-1480, 891-1318, 891-1326, 891-1348, 891-1575, 911-1111, 911-1312, 914-1221, 925-1362, 925-1394, 1001-1290, 1066-1374, 1088-1243, 1113-1296, 1171-1645, 1213-1326, 1319-1556, 1319-1878, 1319-1919, 1351-1921, 1357-1592, 1376-1867, 1390-1921, 1406-1646, 1430-1671, 1478-1725, 1502-1701, 1522-1921, 1558-1917, 1560-1746, 1560-1921, 1587-1795, 1695-1921, 1841-2143, 1847-1921, 1922-2129, 1922-2425, 2000-2203, 2009-2249, 2016-2218, 2016-2313, 2019-2155, 2055-2290, 2096-2381, 2166-2394, 2204-2485, 2204-2486, 2204-2795, 2208-2440, 2208-2444, 2241-2443, 2246-2488, 2246-2831, 2286-2909



Table 4

Polynucleotide SEQ ID NO:/ Incyte ID/ Sequence Length	Sequence Fragments
77/258383CB1/ 2216	1-226, 82-368, 82-513, 82-520, 82-540, 82-557, 82-571, 82-575, 82-610, 82-613, 82-619, 82-626, 82-628, 82-676, 82-734, 83-468, 83-571, 83-634, 88-548, 90-219, 96-381, 98-616, 122-423, 125-562, 168-785, 177-846, 182-513, 184-395, 188-437, 188-723, 188-748, 189-379, 189-663, 189-768, 201-747, 202-1007, 221-578, 234-785, 267-708, 354-910, 388-1073, 397-978, 411-979, 423-964, 437-928, 438-1036, 471-807, 480-1043, 529-962, 537-1184, 560-1084, 574-1077, 592-1010, 593-1073, 651-1084, 654-1066, 654-1084, 658-1252, 662-1343, 699-1196, 760-1319, 781-1449, 807-1067, 807-1309, 811-1082, 864-1121, 937-1235, 939-1495, 1007-1586, 1036-1464, 1072-1356, 1110-1417, 1125-1664, 1134-1691, 1134-1716, 1184-1462, 1184-1465, 1184-1793, 1203-1476, 1233-1424, 1247-1816, 1251-1537, 1366-1929, 1420-1691, 1423-1709, 1595-2216, 1643-2062, 1645-2216, 1669-2216, 1735-2216
78/2804937CB1/ 5320	1-841, 4-671, 292-843, 292-847, 294-643, 329-4681, 436-801, 605-894, 1232-1669, 1471-1741, 1950-2226, 1950-2439, 1950-2443, 1950-2520, 1950-2524, 2113-2740, 2115-2775, 2120-2793, 2213-2798, 2260-2857, 2323-2857, 2347-2870, 2383-3024, 2398-3079, 2429-3142, 2456-3035, 2459-3079, 2508-2838, 2532-3079, 2572-3160, 2599-3079, 2607-3209, 2607-3232, 2620-3219, 2697-3259, 2701-2879, 2701-2994, 2701-3340, 2763-2817, 2779-3422, 2804-3070, 2811-3035, 2831-3243, 2831-3417, 2844-3133, 2861-3369, 2900-3064, 2914-3500, 2974-3256, 3001-3609, 3021-3595, 3032-3535, 3060-3333, 3060-3553, 3065-3337, 3065-3565, 3085-3670, 3087-3678, 3094-3607, 3118-3607, 3118-3727, 3119-3762, 3129-3619, 3130-3693, 3135-3726, 3165-3841, 3166-3623, 3166-3766, 3214-3444, 3219-3809, 3223-3819, 3235-3715, 3240-3879, 3264-3710, 3305-3845, 3306-3820, 3329-3979, 3336-3792, 3339-3972, 3342-4018, 3369-4032, 3370-3890, 3405-3946, 3422-3639, 3432-3927, 3447-3706, 3471-4052, 3471-4124, 3493-4138, 3494-4126, 3496-4105, 3501-3762, 3501-3921, 3502-4028, 3503-4076, 3523-4138, 3556-3829, 3557-3772, 3569-4175, 3578-4188, 3591-3850, 3617-4269, 3621-3827, 3626-4175, 3637-3955, 3643-4208,

Table 4

Polynucleotide SEQ ID NO./ Incyte ID/ Sequence Length	Sequence Fragments
78 (cont.)	3647-4203, 3659-4214, 3663-4155, 3663-4275, 3678-4011, 3682-3950, 3682-4088, 3682-4214, 3695-4268, 3701-4230, 3704-4293, 3717-3955, 3717-4286, 3726-4266, 3731-4312, 3734-4345, 3737-4355, 3749-4344, 3750-4006, 3750-4331, 3751-4011, 3756-4343, 3763-4293, 3780-4272, 3780-4450, 3781-4316, 3786-4056, 3807-4196, 3808-3905, 3809-4469, 3810-4368, 3813-4209, 3816-4344, 3821-4013, 3824-4305, 3831-4422, 3832-4360, 3848-4565, 3855-4565, 3857-4401, 3863-4151, 3863-4216, 3863-4323, 3868-4458, 3870-4509, 3871-4565, 3883-4415, 3886-4495, 3908-4535, 3914-4470, 3915-4384, 3924-4507, 3925-4182, 3934-4236, 3935-4427, 3937-4200, 3942-4356, 3942-4479, 3943-4218, 3946-4232, 3947-4591, 3948-4462, 3948-4591, 3952-4196, 3955-4129, 3961-4547, 3963-4514, 3967-4606, 3974-4608, 3978-4440, 3994-4458, 3997-4385, 3997-4619, 3998-4458, 4007-4470, 4009-4517, 4014-4509, 4017-4625, 4017-4682, 4021-4449, 4029-4599, 4039-4646, 4061-4094, 4062-4609, 4067-4366, 4074-4584, 4076-4659, 4081-4349, 4086-4313, 4086-4589, 4097-4659, 4120-4551, 4122-4741, 4124-4716, 4125-4591, 4135-4670, 4136-4645, 4137-4683, 4142-4709, 4146-4372, 4146-4634, 4146-4692, 4146-4729, 4147-4396, 4153-4715, 4162-4679, 4164-4706, 4169-4639, 4169-4699, 4172-4686, 4180-4403, 4186-4718, 4188-4810, 4192-4842, 4211-4753, 4230-4681, 4244-4672, 4245-4836, 4258-4729, 4263-4622, 4263-4854, 4264-4699, 4275-4830, 4276-4885, 4280-4888, 4288-4534, 4288-4723, 4288-4938, 4289-4895, 4297-4429, 4300-4871, 4312-4657, 4315-4760, 4315-4914, 4327-4753, 4327-4806, 4338-4888, 4340-4761, 4340-4903, 4355-4590, 4357-4565, 4361-4899, 4364-5013, 4374-4899, 4389-4894, 4389-4898, 4390-4903, 4393-4964, 4399-4648, 4399-4895, 4406-4719, 4416-4654, 4416-4664, 4416-4879, 4421-4899, 4434-4902, 4438-4903, 4448-4978, 4471-4903, 4475-5125, 4477-4836, 4494-4853, 4494-4958, 4496-4903, 4502-4901, 4503-4914, 4507-4903, 4510-4902, 4568-4974, 4570-4762, 4573-4903, 4575-4805, 4614-4898, 4651-4903, 4720-4943, 4720-4964, 4722-4893, 4867-5130, 4953-5320, 5018-5269, 5104-5320, 5134-5320, 5155-5320
79/7494915CBI/ 653	1-653, 51-602
80/2073751CBI/ 1794	1-415, 14-312, 14-367, 14-496, 14-507, 14-510, 14-559, 14-560, 19-268, 19-463, 54-340, 62-542, 81-564, 102-560, 110-941, 111-372, 117-369, 117-599, 120-326, 191-508, 199-709, 239-550, 252-731, 532-599, 600-658, 788-1715, 790-1227, 792-1044, 1051-1229, 1082-1227, 1266-1794, 1280-1583, 1395-1544, 1716-1794

Table 4

Polynucleotide SEQ ID NO./ Incyte ID/ Sequence Length	Sequence Fragments
81/3178841CBI/ 2691	1-282, 1-510, 8-281, 53-404, 55-518, 55-519, 58-501, 73-519, 78-447, 86-348, 90-501, 97-886, 115-515, 120-324, 120-446, 120-519, 130-519, 136-387, 136-694, 148-519, 152-519, 160-515, 163-517, 163-519, 168-466, 179-464, 202-510, 265-954, 267-469, 467-1036, 485-1029, 512-970, 514-1021, 515-1164, 516-907, 516-981, 517-1116, 518-1067, 521-905, 521-906, 521-931, 521-946, 521-991, 521-997, 521-1021, 521-1022, 521-1023, 521-1036, 521-1041, 521-1047, 521-1050, 521-1059, 521-1066, 521-1082, 521-1089, 521-1113, 521-1115, 521-1126, 521-1128, 521-1130, 521-1136, 521-1145, 521-1154, 521-1158, 521-1167, 521-1172, 522-1116, 527-1206, 530-871, 530-1209, 543-815, 543-921, 547-867, 547-977, 559-1076, 561-929, 585-1217, 599-882, 613-1267, 619-885, 620-1194, 647-1261, 653-1303, 673-1310, 692-1369, 698-1123, 720-1378, 733-1476, 734-889, 738-1379, 744-1025, 764-1217, 770-1470, 789-985, 793-1470, 794-1304, 800-1055, 813-1416, 834-1496, 871-1568, 883-1152, 883-1163, 883-1649, 905-1471, 925-1475, 937-1203, 1011-1630, 1012-1589, 1031-1512, 1054-1639, 1066-1719, 1120-1606, 1120-1755, 1156-1396, 1157-1755, 1159-1431, 1177-1755, 1184-1388, 1238-1733, 1247-1737, 1248-1805, 1273-1512, 1273-1519, 1273-1527, 1273-1528, 1303-1769, 1346-1906, 1357-1525, 1361-1755, 1430-1727, 1453-1966, 1459-1762, 1466-1755, 1492-2116, 1499-1784, 1501-1805, 1544-2110, 1565-1947, 1580-1967, 1582-1816, 1588-1765, 1605-1771, 1622-2150, 1631-2200, 1655-2263, 1672-1961, 1672-2161, 1717-2229, 1718-1921, 1718-2180, 1730-2225, 1749-2302, 1749-2382, 1751-2005, 1751-2007, 1766-1992, 1776-2037, 1803-2200, 1822-2083, 1856-2292, 1869-2440, 1918-2081, 1939-2549, 1949-2601, 1953-2601, 1968-2397, 1989-2574, 2004-2394, 2009-2536, 2043-2332, 2067-2346, 2068-2333, 2068-2425, 2069-2318, 2069-2417, 2074-2327, 2083-2341, 2112-2378, 2112-2648, 2112-2687, 2132-2442, 2136-2682, 2151-2662, 2167-2380, 2187-2691, 2200-2462, 2207-2486, 2234-2531, 2238-2467, 2417-2579
82/3674807CBI/ 2056	1-290, 1-436, 1-453, 1-456, 1-488, 1-491, 1-524, 1-524, 1-558, 1-563, 1-581, 1-591, 1-598, 1-600, 1-613, 1-641, 1-652, 1-686, 1-754, 2-575, 41-736, 58-502, 83-748, 105-854, 126-911, 133-395, 157-874, 167-650, 197-807, 226-703, 230-807, 265-716, 323-891, 388-1071, 406-708, 417-1080, 440-1053, 441-682, 443-1099, 444-1024, 445-1075, 497-850, 504-1064, 527-1165, 547-1182, 573-1124, 631-1179, 635-1204, 636-1165, 660-1163, 664-1218, 688-864, 716-1206, 719-1339, 723-1023, 752-1255, 759-1295, 771-1325, 773-1382, 778-1378, 795-1382, 800-1455, 804-1354, 811-1272, 823-1461, 834-1202, 837-1525, 845-1438, 846-1296, 850-1224, 857-1058, 866-983, 866-1282, 866-1362, 918-1530, 976-1553, 983-1497, 1009-1446, 1046-1509, 1251-1882, 1388-1888, 1424-1711, 1721-2056, 1754-2056, 1807-2056

Table 4

Polynucleotide SEQ ID NO./ Incyte ID/ Sequence Length	Sequence Fragments
83/1794922CB1/ 2275	1-283, 1-407, 169-592, 169-957, 579-972, 838-1488, 850-1634, 896-1138, 896-1385, 1031-1642, 1084-1347, 1084-1544, 1166-1411, 1357-1649, 1357-1662, 1417-2118, 1459-1655, 1459-1722, 1464-1719, 1464-1996, 1472-2167, 1574-2254, 1575-1878, 1643-1791, 1684-2275, 1739-1994, 1739-2183, 1739-2199, 1765-2246, 1808-2266, 1810-2269, 1816-2265, 1821-2257, 1825-2275, 1844-2265, 1876-2266, 1926-2265, 2042-2275
84/1795509CB1/ 1219	1-282, 1-284, 62-313, 71-271, 72-325, 72-512, 72-826, 100-415, 108-345, 145-648, 167-555, 238-443, 238-943, 240-788, 293-552, 322-845, 337-887, 370-887, 397-685, 443-683, 443-921, 443-943, 469-694, 499-1096, 512-745, 526-717, 530-845, 571-1009, 574-1034, 575-889, 579-1038, 579-1051, 579-1061, 583-1052, 584-845, 651-878, 661-1210, 661-1219, 668-1219, 674-1190, 677-845, 740-1208, 859-1219, 944-1206
85/2017180CB1/ 1015	1-264, 1-305, 1-447, 6-433, 7-515, 7-517, 9-330, 11-615, 15-308, 16-235, 16-293, 18-211, 18-279, 18-295, 20-665, 21-224, 22-375, 26-718, 33-259, 35-300, 35-812, 36-290, 39-504, 40-334, 51-328, 52-287, 52-747, 58-317, 72-686, 79-527, 80-344, 114-677, 145-308, 174-444, 196-465, 228-463, 252-753, 362-768, 439-717, 459-1015, 479-748, 520-657, 527-1012, 557-862, 602-884, 673-1012, 703-994, 706-987, 722-964, 725-976, 725-1015, 731-999, 743-991
86/219442CB1/ 2392	1-408, 1-416, 1-460, 2-384, 4-297, 7-283, 118-745, 158-447, 350-855, 376-855, 381-612, 394-664, 419-855, 441-855, 493-659, 525-1114, 592-855, 629-1263, 635-953, 665-1113, 774-1133, 801-998, 820-1269, 883-1239, 913-1150, 916-1044, 937-1114, 963-1061, 963-1115, 1035-1269, 1096-1628, 1120-1616, 1437-1941, 1617-2266, 1619-1890, 1668-1976, 1691-2045, 1707-2253, 1713-2392, 1787-2080, 1798-2096, 1816-1946, 1818-2392, 1836-2392, 1879-2345, 1901-2392, 1935-2328, 1939-2392, 1944-2328, 1953-2059, 1964-2382
87/2597459CB1/ 1799	1-578, 148-611, 404-1009, 421-824, 427-884, 432-612, 517-1000, 643-847, 643-909, 643-1098, 643-1123, 643-1130, 643-1136, 643-1139, 643-1143, 643-1149, 643-1150, 643-1164, 643-1169, 643-1178, 643-1180, 643-1181, 643-1182, 643-1189, 643-1200, 643-1210, 643-1219, 643-1249, 643-1277, 643-1290, 674-1283, 701-1279, 705-1413, 755-1305, 898-1080, 966-1231, 966-1425, 1018-1711, 1019-1588, 1022-1409, 1052-1630, 1066-1552, 1069-1442, 1119-1713, 1133-1696, 1145-1555, 1165-1754, 1190-1795, 1194-1767, 1202-1743, 1251-1761, 1255-1381, 1262-1789, 1262-1799, 1283-1799, 1314-1440, 1314-1767, 1379-1634, 1384-1599, 1384-1799, 1437-1706, 1444-1727

Table 4

Polynucleotide SEQ ID NO./ Incyte ID/ Sequence Length	Sequence Fragments
88/2783863CB1/ 3718	1-556, 227-772, 270-767, 279-574, 279-823, 279-909, 300-863, 387-977, 468-959, 600-1232, 884-1201, 884-1341, 884-1455, 927-1069, 962-1117, 962-1562, 985-1742, 1007-1525, 1007-1592, 1045-1763, 1066-1448, 1088-1339, 1171-2106, 1183-1451, 1183-1742, 1189-1967, 1250-1897, 1267-1954, 1296-2124, 1301-1449, 1433-2059, 1466-2059, 1560-2297, 1571-1823, 1571-1828, 1606-2363, 1625-1911, 1658-2015, 1664-1905, 1664-1919, 1664-2146, 1676-2352, 1681-1994, 1683-2031, 1686-2246, 1839-2104, 1846-2049, 1850-2069, 1856-2826, 1870-2666, 2056-2233, 2113-2365, 2216-2491, 2218-2823, 2241-2473, 2256-2834, 2256-2881, 2266-2546, 2298-2564, 2330-2618, 2336-2618, 2341-2784, 2363-2604, 2377-2897, 2387-2902, 2402-2646, 2402-2671, 2402-2954, 2450-2733, 2456-2875, 2503-2721, 2512-2973, 2627-2889, 2644-2908, 2741-2973, 2755-3289, 2816-3209, 2836-3387, 2847-3655, 2895-3151, 2896-3466, 2912-3158, 2945-3180, 2970-3262, 2971-3224, 2985-3710, 2987-3274, 3063-3718, 3064-3675, 3106-3636, 3116-3710, 3117-3695, 3139-3704, 3143-3712, 3192-3700, 3200-3496, 3201-3712, 3215-3664, 3227-3699, 3228-3645, 3248-3711, 3249-3711, 3252-3710, 3258-3710, 3305-3665, 3356-3599, 3356-3696, 3356-3710, 3372-3707, 3407-3594, 3407-3605, 3407-3707, 3413-3664, 3426-3711, 3429-3707
89/2902971CB1/ 3250	1-105, 1-622, 1-644, 2-200, 2-285, 2-287, 2-821, 4-273, 8-232, 8-254, 8-256, 8-282, 8-635, 13-251, 16-236, 18-138, 18-284, 18-303, 18-313, 19-812, 29-673, 34-231, 34-232, 34-282, 34-842, 43-482, 61-274, 64-266, 65-266, 68-266, 102-650, 200-274, 208-258, 276-582, 327-501, 575-1157, 665-838, 665-1384, 784-932, 803-1417, 848-1665, 855-1472, 908-1530, 1013-1615, 1030-1345, 1041-1266, 1123-1527, 1157-1611, 1160-1737, 1293-1535, 1403-1721, 1450-2069, 1466-1710, 1631-1749, 1631-2071, 1700-1983, 1739-2028, 1739-2180, 1809-2254, 1844-2278, 1897-2310, 1959-2199, 1959-2477, 1959-2491, 1971-2250, 2001-2477, 2043-2477, 2043-2516, 2050-2477, 2063-2477, 2165-2362, 2165-2603, 2165-2783, 2285-2980, 2363-2748, 2364-2975, 2394-2659, 2467-3133, 2477-3163, 2478-2936, 2478-2978, 2536-2807, 2604-2987, 2623-2875, 2623-2907, 2623-2911, 2623-2924, 2625-2944, 2678-3224, 2698-3219, 2755-3204, 2766-3237, 2775-3250, 2789-3062, 2789-3217, 2789-3222, 2792-3245, 2801-3242, 2812-3237, 2828-3237, 2845-3235, 2849-3228, 2897-3231, 2923-3131, 2953-3250
90/368660CB1/ 2295	1-584, 4-273, 7-286, 33-410, 34-790, 35-811, 41-548, 529-1215, 530-935, 584-1232, 648-1227, 653-1394, 654-1118, 684-1187, 795-1048, 923-1158, 928-1227, 928-1415, 958-1196, 1016-1265, 1017-1325, 1038-1309, 1163-1368, 1172-1542, 1388-1705, 1473-1557, 1477-1691, 1482-1774, 1485-2117, 1489-1747, 1526-2130, 1569-1748, 1658-2186, 1712-1917, 1712-1931, 1712-1934, 1712-1936, 1712-1947, 1712-1965, 1712-1982, 1714-2190, 1720-1853, 1728-2295, 1740-1996, 1754-2252, 1777-1984, 1779-2042, 1791-2051, 1853-2031, 1863-1997, 1920-2293, 1922-2295

Table 4

Polynucleotide SEQ ID NO./ Incye ID/ Sequence Length	Sequence Fragments
91/2804990CB1/ 1777	1-738, 1-780, 210-758, 214-1734, 414-722, 484-517, 495-743, 498-884, 518-801, 641-1240, 679-975, 735-1131, 743-1234, 763-1285, 847-1458, 868-1191, 918-1186, 973-1353, 1041-1348, 1041-1452, 1094-1432, 1154-1594, 1202-1395, 1214-1614, 1214-1718, 1218-1688, 1218-1710, 1218-1747, 1222-1487, 1222-1689, 1222-1746, 1253-1478, 1255-1777, 1266-1720, 1270-1594, 1271-1594, 1273-1594, 1279-1550, 1282-1552
92/168571CB1/ 3181	1-564, 1-591, 50-722, 177-780, 382-983, 404-661, 426-1056, 444-979, 543-1149, 599-1147, 648-1148, 682-1146, 687-1146, 689-1139, 909-1605, 1150-1412, 1150-1567, 1150-1611, 1152-1417, 1157-1765, 1159-1624, 1159-1666, 1159-1759, 1159-1760, 1168-1625, 1196-1449, 1216-1550, 1291-1505, 1291-1541, 1322-1737, 1331-1542, 1579-1793, 1601-1967, 1707-2028, 1717-1942, 1781-2282, 1800-2145, 1836-2063, 1839-2077, 1839-2409, 1865-2430, 1875-2369, 1952-2369, 1960-2574, 1960-2593, 1961-2169, 1968-2611, 1971-2361, 1975-2558, 1979-2167, 1999-2656, 2019-2298, 2021-2406, 2021-2476, 2022-2241, 2022-2559, 2062-2304, 2079-2271, 2112-2382, 2128-2715, 2133-2685, 2160-2672, 2185-2509, 2204-2808, 2222-2644, 2223-2814, 2293-2571, 2303-2523, 2305-2868, 2329-2576, 2334-2606, 2335-2628, 2341-2856, 2379-2693, 2417-2638, 2425-2727, 2472-2896, 2494-3097, 2495-2724, 2500-2696, 2500-2772, 2500-2781, 2500-2835, 2500-3078, 2501-2773, 2504-3008, 2519-3171, 2540-2851, 2544-2861, 2565-2827, 2567-2786, 2579-3101, 2583-2744, 2586-2885, 2586-3094, 2588-3102, 2602-2863, 2607-2859, 2648-2863, 2649-2814, 2664-3165, 2671-3161, 2708-3002, 2749-3094, 2800-3180, 2821-3098, 2821-3116, 2902-3149, 3025-3181
93/1286391CB1/ 5987	1-650, 1-2676, 152-347, 266-860, 266-968, 362-528, 442-4155, 634-1105, 660-901, 823-1005, 823-1263, 1004-1581, 1104-1337, 1126-1735, 1207-1630, 1229-1926, 1324-2013, 1415-1659, 1415-1728, 1838-2104, 1872-2353, 1959-2529, 2093-2721, 2111-2647, 2132-2438, 2177-2678, 2233-2705, 2331-3122, 2352-2542, 2447-2678, 2491-3289, 2537-3129, 2704-3268, 2729-3009, 2729-3192, 2729-3194, 2729-3279, 2729-3292, 2805-3377, 2822-3285, 2875-3573, 2893-3549, 3028-3710, 3060-3611, 3079-3290, 3114-3527, 3256-3902, 3281-3856, 3297-3848, 3331-3838, 3336-3851, 3364-3863, 3438-3903, 3439-4143, 3545-4169, 3603-4056, 3603-4252, 3698-4456, 3701-4276, 3742-4452, 3743-4167, 3743-4326, 3743-4360, 3743-4365, 3743-4411, 3743-4424, 3743-4427, 3743-4458, 3743-4487, 3747-3967, 3763-4251, 3780-4419, 3790-4053, 3790-4220, 3804-4498, 3807-4424, 3887-4391, 3888-4502, 3894-4451, 3896-4502, 3928-4074, 3928-4156, 3928-4499, 3930-4380, 3933-4609, 3961-4662, 3986-4244, 3991-4459, 3992-4629, 3999-4529, 4025-4577, 4054-4691, 4054-4709, 4145-4184, 4193-4757, 4350-4878, 4350-5055, 4350-5067, 4351-5002, 4490-5197, 4490-5265, 4532-5209, 4545-5117, 4563-5157, 4592-5083, 4646-5278,

Table 4

Polynucleotide SEQ ID NO./ Incyte ID/ Sequence Length	Sequence Fragments
93 (cont.)	4650-5278, 4652-5315, 4683-5357, 4684-5339, 4709-5193, 4715-5341, 4720-5399, 4731-5400, 4732-5395, 4744-5220, 4756-5348, 4763-5378, 4785-5413, 4788-5078, 4788-5281, 4788-5309, 4788-5383, 4788-5472, 4788-5491, 4789-5386, 4789-5395, 4791-5425, 4792-5440, 4798-5064, 4798-5363, 4799-5383, 4799-5491, 4799-5584, 4800-5349, 4801-5607, 4818-5087, 4823-5300, 4831-5288, 4844-5125, 4844-5320, 4845-5032, 4861-5409, 4897-5514, 4898-5493, 4899-5527, 4906-5384, 4910-5163, 4910-5578, 4914-5480, 4914-5493, 4915-5158, 4915-5503, 4920-5527, 4921-5496, 4936-5650, 4939-5221, 4942-5449, 4946-5535, 4949-5559, 4950-5527, 4954-5455, 4954-5536, 4956-5501, 4964-5597, 4965-5565, 4967-5599, 4980-5564, 4999-5483, 5001-5457, 5002-5527, 5018-5556, 5021-5274, 5024-5534, 5040-5564, 5042-5514, 5061-5522, 5068-5539, 5070-5696, 5140-5371, 5232-5942, 5311-5977, 5327-5981, 5331-5987, 5336-5977, 5336-5955, 5485-5987, 5572-5981, 5629-5743, 5629-5920, 5684-5905, 5688-5920, 5753-5965, 5766-5920
94/2007684CB1/ 765	1-275, 1-536, 23-227, 55-580, 250-765, 345-610, 420-765, 451-759, 452-613, 474-613
95/2227040CB1/ 2674	1-418, 123-418, 162-484, 167-671, 187-391, 428-651, 524-764, 524-769, 524-1060, 552-667, 601-952, 797-1050, 797-1336, 840-1091, 1023-1444, 1034-1555, 1104-1684, 1149-1369, 1149-1626, 1301-1416, 1310-1545, 1318-1546, 1506-2099, 1661-2031, 1662-1944, 1677-2331, 1705-1968, 1771-2277, 1799-2106, 1901-2385, 1936-2142, 1936-2190, 1936-2208, 1941-2209, 1944-2242, 1944-2247, 1944-2400, 1945-2150, 1968-2192, 1968-2474, 2002-2233, 2035-2674, 2039-2295, 2064-2401, 2071-2639, 2083-2256, 2097-2248, 2101-2671, 2160-2419, 2166-2330, 2166-2377, 2168-2389, 2278-2377, 2290-2377
96/4346130CB1/ 5920	1-479, 2-493, 2-533, 2-535, 2-561, 21-272, 24-400, 30-558, 32-402, 37-480, 179-705, 471-800, 492-789, 536-672, 536-910, 536-1141, 784-1423, 860-1379, 971-1215, 971-1226, 971-1358, 971-1565, 1053-1324, 1137-1485, 1349-1817, 1368-1624, 1368-1841, 1435-1987, 1435-2009, 1561-2121, 1588-1817, 1590-2121, 1600-1817, 1720-1817, 1722-1817, 1768-2170, 2013-2504, 2079-2317, 2079-2346, 2079-2398, 2155-2682, 2155-2738, 2310-5524, 2373-2857, 2451-2684, 2544-3072, 2771-3257, 2948-3187, 3369-4024, 3537-4052, 4366-4776, 4377-4732, 4378-4682, 4413-4693, 4752-5051, 4919-5161, 4945-5574, 5013-5385, 5055-5646, 5070-5319, 5241-5501, 5303-5864, 5392-5780, 5392-5802, 5393-5627, 5431-5684, 5431-5920, 5433-5837, 5469-5873
97/55117040CB1/ 1689	1-341, 1-347, 1-385, 1-418, 1-560, 1-661, 4-661, 5-661, 58-637, 89-157, 89-167, 89-171, 114-823, 200-268, 200-282, 201-282, 225-268, 325-877, 805-1689, 817-1532

Table 4

Polynucleotide SEQ ID NO./ Incyte ID/ Sequence Length	Sequence Fragments
98/7472392CB1/ 1314	1-157, 1-158, 1-195, 1-333, 1-364, 1-438, 1-508, 1-510, 1-513, 1-546, 1-620, 1-624, 1-657, 1-684, 1-721, 1-735, 1-744, 1-764, 1-831, 1-912, 1-1048, 1-1307, 4-548, 14-811, 20-661, 24-920, 76-1044, 80-141, 231-778, 231-782, 342-761, 502-1031, 536-1035, 536-1314, 561-657, 576-973, 648-788
99/4028960CB1/ 3322	1-824, 11-856, 19-545, 97-209, 115-790, 174-777, 174-850, 187-655, 209-534, 396-678, 434-650, 434-950, 657-935, 657-1053, 783-1046, 783-1383, 834-970, 879-1067, 885-1496, 945-1592, 1071-1491, 1176-1337, 1234-1892, 1284-1663, 1293-1801, 1314-1534, 1320-1704, 1341-1953, 1454-1760, 1684-1919, 1684-1920, 1684-1933, 1684-2140, 1690-2148, 1850-2042, 1873-2116, 1875-2098, 1890-2348, 1963-2703, 2027-2518, 2043-2329, 2101-2324, 2127-2372, 2137-2776, 2169-2577, 2218-2493, 2322-2911, 2324-2491, 2336-2994, 2344-2558, 2395-2924, 2403-3035, 2409-2592, 2414-2978, 2415-2688, 2496-2757, 2498-2724, 2505-3038, 2529-2864, 2536-2980, 2562-2692, 2632-3052, 2654-3051, 2743-3233, 2767-3227, 2784-3224, 2787-2921, 2794-3016, 2808-3218, 2817-3050, 2906-3322
100/8227004CB1/ 3621	1-250, 1-434, 1-492, 1-611, 1-612, 1-676, 1-860, 100-900, 114-772, 238-680, 247-879, 273-494, 288-685, 341-1108, 396-813, 402-813, 425-1104, 467-1245, 507-1224, 526-896, 650-1364, 655-1231, 656-1302, 661-1301, 668-1423, 671-1042, 679-1258, 711-1301, 760-1301, 763-1131, 782-1542, 787-1323, 794-1224, 818-1271, 852-1355, 874-1462, 904-1036, 916-1301, 961-1624, 980-1454, 1011-1397, 1025-1592, 1028-1255, 1031-1728, 1065-1298, 1065-1605, 1149-1842, 1168-1548, 1202-1682, 1209-2160, 1217-1697, 1229-1757, 1282-1511, 1313-1804, 1334-2037, 1362-2087, 1372-1967, 1400-2375, 1407-2144, 1497-2162, 1621-2285, 1627-2092, 1627-2569, 1629-2068, 1630-2318, 1652-1880, 1673-2409, 1683-2354, 1708-1979, 1733-1995, 1742-2449, 1743-2000, 1745-2189, 1746-2419, 1751-2439, 1751-2497, 1759-2530, 1792-2108, 1795-2614, 1816-2097, 1834-2105, 1845-2598, 1893-2144, 1893-2485, 1903-2586, 1904-2715, 1904-2732, 1949-2203, 1951-2207, 1975-2296, 1977-2878, 1979-2214, 1980-2645, 1989-2407, 1996-2256, 1999-2668, 2006-2722, 2025-2560, 2032-2514, 2046-2745, 2061-2540, 2079-2707, 2094-2348, 2094-2895, 2106-2296, 2106-2510, 2109-2289, 2109-2597, 2112-2372, 2119-2385, 2138-2789, 2150-2447, 2174-2333, 2188-2889, 2195-2841, 2209-2802, 2216-2546, 2251-2596, 2251-2604, 2272-2527, 2296-2583, 2297-2575, 2312-2811, 2321-2574, 2335-2664, 2343-2950, 2350-2865, 2351-2879, 2353-2827, 2355-2567, 2363-2759, 2390-2588, 2394-2664, 2421-2920, 2426-2740, 2427-2942, 2447-2862, 2458-2846, 2462-3141, 2466-2720, 2470-3192, 2483-2699, 2483-2997, 2798-3256, 2859-3106, 2908-3175, 2921-3178, 3049-3309, 3049-3621



Table 4

Polynucleotide SEQ ID NO./ Incyte ID/ Sequence Length	Sequence Fragments
101/3044763CB1/ 2704	1-283, 41-819, 66-368, 88-204, 215-856, 218-734, 303-647, 389-661, 421-706, 465-713, 482-1060, 490-610, 490-952, 511-1108, 516-1026, 569-1199, 576-1240, 585-1112, 673-1246, 677-1221, 697-974, 732-978, 742-1290, 755-1049, 780-1430, 824-997, 844-1079, 872-1392, 913-1188, 946-1561, 979-1529, 1035-1304, 1035-1755, 1035-1818, 1039-1294, 1056-1207, 1056-1290, 1076-1758, 1111-1489, 1113-1375, 1117-1433, 1147-1515, 1162-1458, 1166-1744, 1171-1427, 1172-1518, 1173-1393, 1191-1461, 1208-1511, 1217-1365, 1227-1537, 1249-1800, 1273-1923, 1290-1513, 1296-1547, 1302-1495, 1321-1409, 1324-1798, 1332-1627, 1341-1494, 1341-1623, 1343-1818, 1363-1682, 1363-1886, 1380-1649, 1388-1631, 1390-1635, 1390-1822, 1392-1911, 1397-1818, 1400-1818, 1402-1734, 1419-1791, 1420-1799, 1429-1818, 1438-1714, 1460-1646, 1461-1677, 1503-1918, 1511-1897, 1522-1608, 1556-1799, 1571-1818, 1577-2418, 1596-1818, 1637-1918, 1643-1878, 1658-1808, 1658-1818, 1660-2116, 1754-1860, 1757-1813, 1757-1818, 1760-1918, 2110-2704
102/4044519CB1/ 1345	1-146, 1-291, 1-490, 1-574, 1-583, 1-598, 1-627, 1-631, 1-657, 1-679, 1-680, 1-808, 92-804, 98-820, 159-495, 479-1252, 509-1289, 615-1345, 674-1329, 684-1341, 764-1342
103/71351918CB1/ 1607	1-246, 27-253, 29-80, 30-304, 33-278, 33-376, 33-561, 34-225, 36-571, 38-280, 43-324, 60-315, 61-286, 169-738, 308-578, 419-947, 423-659, 424-695, 441-1112, 444-972, 466-994, 468-793, 478-829, 490-798, 498-1124, 506-725, 512-1016, 516-946, 519-791, 545-1040, 547-997, 565-1145, 568-849, 570-813, 570-956, 571-965, 576-736, 579-1111, 581-1028, 582-1167, 587-1142, 588-1208, 595-1145, 595-1378, 596-857, 600-1109, 614-1186, 624-1220, 628-848, 633-1213, 638-1225, 640-1172, 641-1244, 648-822, 648-1403, 649-955, 659-756, 672-1106, 676-1403, 678-949, 680-1192, 683-931, 684-1206, 684-1228, 693-976, 699-1040, 700-960, 711-1305, 715-1263, 726-1304, 730-987, 730-1358, 742-1339, 748-1399, 757-1264, 760-1244, 770-992, 771-1131, 787-1301, 788-1014, 796-1301, 798-1336, 814-1374, 825-1536, 832-1068, 838-1396, 843-1044, 846-1093, 846-1482, 858-1114, 860-1494, 866-1149, 866-1428, 867-1306, 875-1471, 876-1120, 878-1146, 879-1238, 883-1528, 890-1533, 893-1090, 897-1393, 899-1127, 899-1546, 900-1203, 904-1281, 917-1364, 918-1430, 928-1371, 930-1544, 937-1540, 949-1444, 952-1414, 952-1537, 955-1527, 956-1081, 963-1533, 988-1106, 990-1264, 999-1540, 1003-1459, 1006-1539,
	1014-1473, 1015-1415, 1025-1288, 1028-1543, 1028-1550, 1030-1539, 1043-1527, 1046-1317, 1047-1358, 1047-1367, 1047-1607, 1050-1546, 1051-1475, 1058-1353, 1070-1316

Table 4

Polynucleotide SEQ ID NO./ Incyte ID/ Sequence Length	Sequence Fragments
104/8109363CB1/ 2622	1-521, 125-498, 246-543, 268-746, 315-549, 367-885, 403-1139, 464-717, 634-903, 662-1255, 704-925, 742-1371, 845-1124, 864-1385, 966-1471, 1041-1444, 1045-1444, 1105-1415, 1105-1618, 1320-1624, 1320-1888, 1361-1648, 1373-1884, 1448-1688, 1556-1811, 1584-2049, 1591-1840, 1596-2174, 1690-1962, 1697-1956, 1697-2207, 1701-1826, 1772-2051, 1790-2055, 1935-2190, 1937-2617, 2003-2253, 2003-2302, 2003-2490, 2010-2236, 2010-2309, 2011-2622, 2012-2593, 2052-2318, 2063-2292, 2063-2296, 2087-2622, 2094-2616, 2096-2340, 2161-2424, 2254-2510
105/1272746CB1/ 3489	1-214, 1-254, 1-595, 3-267, 7-248, 41-267, 46-275, 154-268, 202-394, 202-775, 202-841, 207-392, 207-534, 207-918, 340-632, 340-866, 401-1133, 463-1095, 506-1225, 592-864, 746-1357, 748-1382, 772-1095, 929-1193, 954-1410, 959-1425, 1059-1554, 1064-1421, 1166-1419, 1336-1669, 1449-1951, 1493-2128, 1519-1968, 1519-2004, 1519-2045, 1519-2055, 1519-2096, 1519-2113, 1519-2155, 1519-2161, 1519-2202, 1520-2009, 1521-1786, 1560-2144, 1569-2178, 1625-2247, 1642-1783, 1663-1912, 1700-2520, 1710-2140, 1734-2263, 1813-2446, 1860-2519, 1880-2572, 1937-2098, 1951-2552, 1953-2706, 1955-2186, 1955-2219, 1955-2641, 1955-2763, 1956-2325, 1959-2420, 1965-2559, 1976-2243, 1982-2480, 1994-2072, 2023-2579, 2024-2647, 2031-2642, 2052-2697, 2053-2742, 2126-2775, 2127-2699, 2135-2420, 2139-2833, 2173-2730, 2177-2840, 2182-2783, 2183-2869, 2215-2456, 2215-2830, 2229-2785, 2236-2935, 2242-2935, 2246-2852, 2256-3027, 2257-2763, 2288-2848, 2294-2924, 2296-2932, 2301-2525, 2314-2824, 2322-2524, 2322-2792, 2324-2935, 2341-2935, 2344-2914, 2354-2935, 2358-2935, 2373-2932, 2379-2932, 2382-2935, 2384-2918, 2386-2599, 2386-2935, 2389-2935, 2391-3001, 2397-2693, 2413-2639, 2422-2935, 2424-2935, 2431-2679, 2443-3079, 2449-2935, 2468-3177, 2477-2941, 2487-2856, 2495-2935, 2499-2932, 2516-2932, 2524-3136, 2526-2932, 2530-2938, 2558-2935, 2561-2935, 2609-3294, 2620-3315, 2621-2940, 2624-2907, 2648-2773, 2658-3455, 2674-3489, 2708-3463, 2756-3191, 2768-2977, 2768-3252, 2768-3265, 2768-3267, 2768-3278, 2768-3288, 2768-3372, 2830-3068, 2830-3195, 2833-3452, 2867-3421, 2889-3431, 2916-3366, 2941-3196, 2962-3443, 2977-3197, 2992-3444, 3020-3285, 3105-3349, 3105-3434, 3105-3452, 3122-3330, 3125-3443, 3126-3449, 3137-3306, 3228-3443, 3230-3443, 3305-3449
106/1839974CB1/ 2269	1-747, 1-757, 24-624, 25-529, 25-530, 87-694, 150-944, 179-571, 313-528, 458-1022, 469-1197, 588-930, 820-1097, 893-1455, 1174-1547, 1174-1604, 1179-1519, 1362-1636, 1447-1743, 1513-1804, 1521-1764, 1654-2269, 1658-1892, 1658-2148, 1661-2231, 1812-2269, 1905-2103, 1912-2175, 1949-2240, 2008-2098

Table 4

Polynucleotide SEQ ID NO:// Incyte ID/ Sequence Length	Sequence Fragments
107/1877336CB1/ 3075	1-194, 1-197, 1-399, 3-412, 4-295, 7-222, 9-240, 13-569, 13-608, 15-558, 15-642, 17-218, 19-628, 25-277, 25-549, 33-305, 34-614, 38-621, 43-698, 102-510, 103-770, 103-800, 112-738, 137-754, 138-429, 144-664, 173-730, 241-514, 259-535, 262-614, 262-662, 286-594, 421-648, 573-1015, 641-1229, 691-1147, 713-942, 725-1421, 757-1368, 803-1368, 806-1309, 820-1492, 835-1360, 835-1368, 837-1459, 840-1325, 844-1339, 872-1439, 877-1464, 883-1467, 889-1366, 893-1557, 895-1366, 898-1370, 926-1593, 959-1455, 971-1387, 1007-1678, 1014-1567, 1045-1572, 1075-1707, 1097-1225, 1104-1471, 1104-1662, 1104-1698, 1106-1800, 1154-1653, 1156-1735, 1160-1850, 1176-1709, 1176-1859, 1177-1806, 1180-1801, 1183-1718, 1196-1800, 1215-1736, 1224-1878, 1252-1897, 1265-1829, 1272-1801, 1283-1639, 1291-1815, 1295-1830, 1314-1866, 1316-1807, 1318-1861, 1319-1795, 1319-1908, 1325-1836, 1335-1848, 1335-1851, 1338-1941, 1340-1905, 1346-1784, 1347-1867, 1355-1820, 1359-1851, 1363-1859, 1379-1947, 1384-1891, 1406-1927, 1417-1902, 1436-2104, 1500-2058, 1519-1981, 1520-2025, 1520-2034, 1521-1859, 1521-1860, 1526-2061, 1528-2160, 1529-2025, 1548-2212, 1557-2158, 1562-2158, 1567-2301, 1591-2113, 1598-2183, 1606-2125, 1610-2247, 1612-2157, 1612-2186, 1628-2291, 1647-2255, 1675-2326, 1684-2069, 1684-2301, 1687-2349, 1699-2148, 1700-2215, 1700-2252, 1704-2212, 1705-2205, 1705-2360, 1738-2370, 1743-2076, 1750-1776, 1752-2278, 1762-2337, 1763-2190, 1763-2285, 1764-2236, 1777-2503, 1791-2295, 1793-2186, 1794-2364, 1800-2361, 1805-2226, 1815-2085, 1819-2382, 1831-2323, 1842-2302, 1873-2325, 1988-2212, 2005-2608, 2039-2706, 2085-2673, 2323-2357, 2365-2695, 2397-2962, 2402-2686, 2418-2677, 2419-2999, 2420-2670, 2430-2668, 2448-2678, 2449-2612, 2457-2660, 2603-2663, 2702-2789, 2704-3056, 2716-2984, 2723-3056, 2729-3057, 2736-2912, 2738-2981, 2762-2997, 2769-2974, 2769-3013, 2769-3027, 2777-3057, 2784-3024, 2785-3058, 2789-3029, 2801-3018, 2811-3056, 2811-3075, 2822-3049, 2823-3049, 2829-3055, 2831-3075, 2833-3039, 2834-3059, 2845-3058, 2851-3061, 2851-3075, 2852-3027, 2852-3046, 2861-3075, 2865-3059, 2865-3075, 2867-3037, 2868-3075, 2876-3046, 2876-3056, 2876-3059, 2876-3073, 2877-3056, 2878-3039, 2879-3058, 2881-2987, 2883-3063, 2885-3032, 2885-3075, 2887-3056, 2887-3058, 2887-3073, 2887-3075, 2890-2989, 2892-3058, 2894-3075, 2895-3042, 2908-3060, 2949-3075, 2998-3057, 2998-3060, 2998-3063, 2998-3064, 2999-3075
108/2321054CB1/ 849	1-96, 1-109, 1-134, 1-273, 100-364, 100-637, 100-656, 100-691, 100-700, 100-831, 100-834, 100-848, 101-453, 132-842, 174-823, 200-731, 200-784, 213-780, 246-833, 273-573, 278-849, 287-796, 297-831, 323-537, 323-553, 334-838, 355-642, 360-587, 361-696, 382-652, 554-776

Table 4

Polynucleotide SEQ ID NO./ Incyte ID/ Sequence Length	Sequence Fragments
109/2796034CB1/ 2659	1-790, 49-773, 85-773, 118-773, 300-773, 326-773, 498-773, 544-799, 563-804, 608-810, 709-1077, 801-1077, 947-1142, 958-1273, 958-1538, 991-1142, 1008-1219, 1262-2658, 1263-1551, 1408-1997, 1479-1860, 1715-2350, 2017-2618, 2156-2306, 2187-2659
110/4413112CB1/ 2205	1-268, 1-289, 1-622, 10-245, 10-358, 10-433, 10-438, 15-263, 367-623, 367-779, 367-816, 367-884, 367-889, 367-897, 367-942, 367-944, 367-947, 367-955, 367-1001, 367-1010, 367-1026, 367-1064, 367-1089, 370-982, 372-464, 382-1075, 458-737, 458-1128, 653-1316, 713-981, 769-1212, 802-1467, 823-1343, 901-1468, 949-1164, 949-1167, 950-1323, 964-1578, 1031-1397, 1034-1650, 1040-1500, 1094-1394, 1129-1804, 1310-1503, 1362-1621, 1416-1512, 1436-1691, 1462-1667, 1462-1717, 1462-1964, 1467-1778, 1478-1619, 1504-1800, 1545-1912, 1611-1837, 1611-2115, 1657-1911, 1703-2205, 1762-2018
111/7654832CB1/ 3042	1-391, 1-567, 29-488, 29-678, 97-699, 104-846, 115-227, 153-627, 153-680, 153-684, 153-726, 153-769, 153-776, 648-942, 649-814, 649-1187, 713-1409, 733-1267, 951-1546, 1107-1800, 1207-1869, 1207-1901, 1207-1938, 1207-1945, 1207-1947, 1207-1981, 1207-1982, 1207-1987, 1207-1994, 1207-1996, 1207-1999, 1208-1938, 1208-1943, 1208-2086, 1274-2012, 1600-1872, 1668-1940, 1668-2141, 1668-2353, 1669-2432, 1819-2113, 1858-2031, 2050-2567, 2051-2327, 2120-2973, 2121-2428, 2135-2973, 2139-2975, 2311-2951, 2393-3009, 2412-3042, 2416-3042, 2423-2949, 2439-3039, 2446-2973, 2460-3009, 2483-2728, 2552-2800, 2559-3042, 2630-2862, 2770-3027
112/7503849CB1/ 2112	1-214, 1-216, 1-249, 1-273, 1-293, 2-239, 4-783, 6-301, 6-343, 8-2112, 10-556, 13-311, 14-303, 14-495, 16-264, 16-633, 17-295, 18-248, 18-269, 18-605, 18-707, 19-252, 19-258, 19-287, 19-536, 19-712, 20-272, 20-374, 21-268, 21-292, 21-328, 21-337, 21-343, 21-444, 22-325, 22-416, 22-703, 23-298, 23-540, 23-641, 24-219, 24-456, 25-687, 25-709, 27-335, 28-304, 29-597, 35-626, 37-665, 37-674, 38-538, 38-704, 39-570, 39-625, 40-631, 40-645, 41-685, 41-784, 42-657, 42-757, 43-301, 45-592, 48-630, 48-708, 51-344, 51-418, 51-421, 53-337, 57-489, 58-386, 59-340, 60-311, 61-418, 62-307, 67-387, 89-333, 115-735, 139-404, 141-338, 141-410, 145-383, 164-440, 165-386, 167-414, 180-464, 186-546, 186-607, 211-466, 218-413, 218-721, 219-539, 220-688, 221-310, 221-446, 230-520, 230-556, 232-485, 235-531, 236-770, 239-874, 278-497, 288-765, 297-748, 314-737, 329-508, 334-580, 384-510, 531-1073, 563-833, 656-945, 674-907, 698-1310, 882-1475, 948-1177, 950-1399, 969-1314, 980-1554, 1012-1252, 1016-1515, 1028-1678, 1030-1298, 1035-1615, 1045-1301, 1047-1501, 1048-1284, 1048-1344, 1056-1684, 1058-1328, 1058-1330, 1058-1336, 1060-1298, 1062-1799, 1066-1582, 1080-1643, 1083-1800, 1091-1668, 1091-1712,

Table 4

Polynucleotide SEQ ID NO./ Incyte ID/ Sequence Length	Sequence Fragments
112 (cont.)	1092-1335, 1098-1657, 1101-1826, 1109-1560, 1109-1624, 1126-1590, 1134-1753, 1137-1590, 1148-1587, 1152- 1586, 1153-1715, 1159-1762, 1168-1314, 1170-1437, 1170-1735, 1172-1789, 1172-1871, 1177-1431, 1177-1474, 1177-1791, 1179-1651, 1190-1636, 1192-1713, 1204-1466, 1205-1628, 1206-1470, 1206-1586, 1219-1584, 1221- 1489, 1225-1628, 1226-1468, 1232-1590, 1234-1467, 1234-1632, 1240-1590, 1240-1800, 1241-1497, 1241-1537, 1241-1587, 1242-1712, 1244-1485, 1246-1427, 1246-1491, 1248-1836, 1249-1708, 1249-1873, 1253-1712, 1255- 1865, 1260-1546, 1266-1712, 1268-1592, 1268-1873, 1270-1497, 1270-1712, 1275-1717, 1275-1718, 1277-1647, 1284-1541, 1295-1826, 1298-1873, 1299-1873, 1300-1715, 1300-1871, 1300-1873, 1302-1873, 1303-1710, 1303- 1785, 1307-1871, 1308-1870, 1316-1536, 1316-1868, 1319-1718, 1321-1858, 1324-1590, 1324-1864, 1325-1866, 1343-1872, 1344-1463, 1345-1583, 1360-1586, 1360-1715, 1379-1676, 1382-1873, 1402-1873, 1415-1873, 1424- 1494, 1424-1873, 1428-1590, 1428-1729, 1428-1873, 1429-1873, 1441-1712, 1441-1872, 1453-1673, 1456-1873, 1458-1873, 1461-2112, 1462-1873, 1463-1872, 1464-1850, 1464-1873, 1476-1871, 1476-1872, 1479-1736, 1483- 1834, 1490-1570, 1490-1873, 1493-1811, 1496-1872, 1502-1861, 1520-1796, 1521-1820, 1528-1658, 1530-1873, 1533-1873, 1534-1822, 1534-1830, 1534-1872, 1548-1872, 1554-1873, 1556-1813, 1557-1872, 1563-1704, 1564- 1872, 1571-1872, 1573-1873, 1599-1868, 1601-1844, 1601-1845, 1624-1873, 1701-1873, 1748-1859, 1814-1864

Table 5

Polynucleotide SEQ ID NO:	Incye Project ID:	Representative Library
57	2867236CB1	KIDNNOT20
58	1294096CB1	PROSTUS23
59	7238537CB1	BRAITUT03
60	7494391CB1	SINTNOT18
61	6451054CB1	CORPNOT02
62	7494592CB1	UTRSTMR01
63	5202657CB1	HEARFET01
64	2013529CB1	TESTNOT03
65	3841351CB1	LIVRNOT21
66	152116CB1	BRAITDR02
67	2381031CB1	PROSBPS05
68	2511371CB1	CONUTUT01
69	8068623CB1	TONSDIC01
70	677977CB1	BRABDIE02
71	1661472CB1	MLP000032
72	1748508CB1	PROSNON01
73	2159545CB1	PLACFEB01
74	8560269CB1	NEUTFMT01
75	8710302CB1	THYMNOE02
76	6778214CB1	THYRTUT03
77	258383CB1	BRSTNOT17
78	2804937CB1	STOMTDE01
80	2073751CB1	TYLMUNT01
81	3178841CB1	UTRSTUE01
82	3674807CB1	PLACNOT07
83	1794922CB1	PROSTUT05
84	1795509CB1	PROSTUT05
85	2017180CB1	BLADTUT08
86	219442CB1	THYMNOT05
87	2597459CB1	BRAKNOK02
88	2783863CB1	BRAHTDR03
89	2902971CB1	BRAVDIN03
90	368660CB1	BRSTNOT01
91	2804990CB1	BRAITUT02
92	168571CB1	BRAUNOR01
93	1286391CB1	MENITUT03
94	2007684CB1	LUNGNON03
95	2227040CB1	BRSTNOT03
96	4346130CB1	BRAUNOR01
98	7472392CB1	BRALNON02
99	4028960CB1	KIDNFEC01
100	8227004CB1	PROSNOT19
101	3044763CB1	HEAANOT01
102	4044519CB1	LUNGNOT35
103	71351918CB1	BRSTTUT01
104	8109363CB1	BRAINOT19
105	1272746CB1	TESTTUT02
106	1839974CB1	OVARDIR01
107	1877336CB1	ADRETUR01

Table 5

Polynucleotide SEQ ID NO:	Incyte Project ID:	Representative Library
108	2321054CB1	BRSTNOT13
109	2796034CB1	LUNGDIN02
110	4413112CB1	MONOTXT01
111	7654832CB1	BLADTUT06
112	7503849CB1	KIDNNOT09

Table 6

Library	Vector	Library Description
ADRETUR01	PCDNA2.1	This random primed library was constructed using RNA isolated from left upper pole, adrenal gland tumor tissue removed from a 52-year-old Caucasian male during nephroureterectomy and local destruction of renal lesion. Pathology indicated grade 3 adrenal cortical carcinoma forming a mass that infiltrated almost the whole adrenal parenchyma and extended to adjacent adipose tissue. A metastatic tumor nodule was identified in the hilar region. The renal vein was infiltrated by tumor and the neoplastic process was present at the resection margin of the renal vein. Fragments of adrenal cortical carcinoma and thrombus were found in the inferior vena cava. Patient history included abnormal weight loss. Family history included skin cancer, type I diabetes, and neurotic depression.
BLADTUT06	pINCY	Library was constructed using RNA isolated from bladder tumor tissue removed from the posterior bladder wall of a 58-year-old Caucasian male during a radical cystectomy, radical prostatectomy, and gastrectomy. Pathology indicated grade 3 transitional cell carcinoma in the left lateral bladder wall. The remaining bladder showed marked cystitis with scattered microscopic foci of transitional cell carcinoma in situ. Patient history included angina, emphysema and tobacco use. Family history included acute myocardial infarction, atherosclerotic coronary artery disease, and type II diabetes.
BLADTUT08	pINCY	Library was constructed using RNA isolated from bladder tumor tissue removed from a 72-year-old Caucasian male during a radical cystectomy and prostatectomy. Pathology indicated an invasive grade 3 (of 3) transitional cell carcinoma in the right bladder base. Patient history included pure hypercholesterolemia and tobacco abuse. Family history included myocardial infarction, cerebrovascular disease, and brain cancer.
BRABDIE02	pINCY	This 5' biased random primed library was constructed using RNA isolated from diseased cerebellum tissue removed from the brain of a 57-year-old Caucasian male who died from a cerebrovascular accident. Serologies were negative. Patient history included Huntington's disease, emphysema, and tobacco abuse (3-4 packs per day, for 40 years).



Table 6

Library	Vector	Library Description
BRACNOK02	PSPORT1	This amplified and normalized library was constructed using RNA isolated from posterior cingulate tissue removed from an 85-year-old Caucasian female who died from myocardial infarction and retroperitoneal hemorrhage. Pathology indicated atherosclerosis, moderate to severe, involving the circle of Willis, middle cerebral, basilar and vertebral arteries; infarction, remote, left dentate nucleus; and amyloid plaque deposition consistent with age. There was mild to moderate leptomeningeal fibrosis, especially over the convexity of the frontal lobe. There was mild generalized atrophy involving all lobes. The white matter was mildly thinned. Cortical thickness in the temporal lobes, both maximal and minimal, was slightly reduced. The substantia nigra pars compacta appeared mildly depigmented. Patient history included COPD, hypertension, and recurrent deep venous thrombosis. 6.4 million independent clones from this amplified library were normalized in one round using conditions adapted from Soares et al., PNAS (1994) 91:9228-9232 and Bonaldo et al., Genome Research 6 (1996):791.
BRAHTDR03	PCDNA2.1	This random primed library was constructed using RNA isolated from archaocortex, anterior hippocampus tissue removed from a 55-year-old Caucasian female who died from cholangiocarcinoma. Pathology indicated mild meningeal fibrosis predominately over the convexities, scattered axonal spheroids in the white matter of the cingulate cortex and the thalamus, and a few scattered neurofibrillary tangles in the entorhinal cortex and the periaqueductal gray region. Pathology for the associated tumor tissue indicated well-differentiated cholangiocarcinoma of the liver with residual or relapsed tumor. Patient history included cholangiocarcinoma, post-operative Budd-Chiari syndrome, biliary ascites, hydrothorax, dehydration, malnutrition, oliguria and acute renal failure. Previous surgeries included cholecystectomy and resection of 85% of the liver.
BRAINOT19	pINCY	Library was constructed using RNA isolated from diseased brain tissue removed from the left frontal lobe of a 27-year-old Caucasian male during a brain lobectomy. Pathology indicated a focal deep white matter lesion, characterized by marked gliosis, calcifications, and hemosiderin-laden macrophages, consistent with a remote perinatal injury. This tissue also showed mild to moderate generalized gliosis, predominantly subpial and subcortical, consistent with chronic seizure disorder. The left temporal lobe, including the mesial temporal structures, showed focal, marked pyramidal cell loss and gliosis in hippocampal sector CA1, consistent with mesial temporal sclerosis. GFAP was positive for astrocytes. The patient presented with intractable epilepsy, focal epilepsy, hemiplegia, and an unspecified brain injury. Patient history included cerebral palsy, abnormality of gait, and depressive disorder. Family history included brain cancer.

Table 6

Library	Vector	Library Description
BRAITDR02	PCDNA2.1	This random primed library was constructed using RNA isolated from allocortex, neocortex, anterior and frontal cingulate tissue removed from a 55-year-old Caucasian female who died from cholangiocarcinoma. Pathology indicated mild meningeal fibrosis predominately over the convexities, scattered axonal spheroids in the white matter of the cingulate cortex and the thalamus, and a few scattered neurofibrillary tangles in the entorhinal cortex and the periaqueductal gray region. Pathology for the associated tumor tissue indicated well-differentiated cholangiocarcinoma of the liver with residual or relapsed tumor. Patient history included cholangiocarcinoma, post-operative Budd-Chiari syndrome, biliary ascites, hydrothorax, dehydration, malnutrition, oliguria and acute renal failure. Previous surgeries included cholecystectomy and resection of 85% of the liver.
BRAITUT02	PSPORT1	Library was constructed using RNA isolated from brain tumor tissue removed from the frontal lobe of a 58-year-old Caucasian male during excision of a cerebral meningeal lesion. Pathology indicated a grade 2 metastatic hypernephroma. Patient history included a grade 2 renal cell carcinoma, insomnia, and chronic airway obstruction. Family history included a malignant neoplasm of the kidney.
BRAITUT03	PSPORT1	Library was constructed using RNA isolated from brain tumor tissue removed from the left frontal lobe of a 17-year-old Caucasian female during excision of a cerebral meningeal lesion. Pathology indicated a grade 4 fibrillary giant and small-cell astrocytoma. Family history included benign hypertension and cerebrovascular disease.
BRAALNON02	pINCY	This thalamus tissue library was constructed from 4.24 million independent clones from a thalamus tissue library. Starting RNA was made from thalamus tissue removed from a 35-year-old Caucasian male who died from cardiac failure. Pathology indicated moderate leptomeningeal fibrosis and multiple microinfarctions of the cerebral neocortex. Microscopically, the cerebral hemisphere revealed moderate fibrosis of the leptomeninges with focal calcifications. There was evidence of shrunken and slightly eosinophilic pyramidal neurons throughout the cerebral hemispheres. Scattered throughout the cerebral cortex, there were multiple small microscopic areas of cavitation with surrounding gliosis. Patient history included dilated cardiomyopathy, congestive heart failure, cardiomegaly and an enlarged spleen and liver. The library was normalized in two rounds using conditions adapted from Soares et al., PNAS (1994) 91:9228-9232 and Bonaldo et al., Genome Research (1996) 6:791, except that a significantly longer (48 hours/round) reannealing hybridization was used.

Table 6

Library	Vector	Library Description
BRAUNOR01	pINCY	This random primed library was constructed using RNA isolated from striatum, globus pallidus and posterior putamen tissue removed from an 81-year-old Caucasian female who died from a hemorrhage and ruptured thoracic aorta due to atherosclerosis. Pathology indicated moderate atherosclerosis involving the internal carotids, bilaterally; microscopic infarcts of the frontal cortex and hippocampus; and scattered diffuse amyloid plaques and neurofibrillary tangles, consistent with age. Grossly, the leptomeninges showed only mild thickening and hyalinization along the superior sagittal sinus. The remainder of the leptomeninges was thin and contained some congested blood vessels. Mild atrophy was found mostly in the frontal poles and lobes, and temporal lobes, bilaterally. Microscopically, there were pairs of Alzheimer type II astrocytes within the deep layers of the neocortex. There was increased satellitosis around neurons in the deep gray matter in the middle frontal cortex. The amygdala contained rare diffuse plaques and neurofibrillary tangles. The posterior hippocampus contained a microscopic area of cystic cavitation with hemosiderin-laden macrophages surrounded by reactive gliosis. Patient history included sepsis, cholangitis, post-operative atelectasis, pneumonia CAD, cardiomegaly due to left ventricular hypertrophy, splenomegaly, arteriolonephrosclerosis, nodular colloid goiter, emphysema, CHF, hypothyroidism, and peripheral vascular disease.
BRAYDIN03	pINCY	This normalized library was constructed from 6.7 million independent clones from a brain tissue library. Starting RNA was made from RNA isolated from diseased hypothalamus tissue removed from a 57-year-old Caucasian male who died from a cerebrovascular accident. Patient history included Huntington's disease and emphysema. The library was normalized in 2 rounds using conditions adapted from Soares et al., PNAS (1994) 91:9228 and Bonaldo et al., Genome Research (1996) 6:791, except that a significantly longer (48 -hours/round) reannealing hybridization was used. The library was linearized and recircularized to select for insert containing clones.
BRSTNOT01	PBLUESCRIPT	Library was constructed using RNA isolated from the breast tissue of a 56-year-old Caucasian female who died in a motor vehicle accident.
BRSTNOT03	PSPORT1	Library was constructed using RNA isolated from diseased breast tissue removed from a 54-year-old Caucasian female during a bilateral radical mastectomy. Pathology for the associated tumor tissue indicated residual invasive grade 3 mammary ductal adenocarcinoma. Patient history included kidney infection and condyloma acuminatum. Family history included benign hypertension, hyperlipidemia and a malignant neoplasm of the colon.

Table 6

Library	Vector	Library Description
BRSTNOT13	pINCY	Library was constructed using RNA isolated from breast tissue removed from a 36-year-old Caucasian female during bilateral simple mastectomy. Patient history included a breast neoplasm, depressive disorder, hyperlipidemia, and a chronic stomach ulcer. Family history included a cardiovascular and cerebrovascular disease; hyperlipidemia; skin, breast, esophageal, bladder, and bone cancer; and Hodgkin's lymphoma.
BRSTNOT17	pINCY	Library was constructed using RNA isolated from breast tissue removed from a 46-year-old Caucasian female during a unilateral extended simple mastectomy. Pathology for the associated tumor tissue indicated invasive grade 3, nuclear grade 2 adenocarcinoma, ductal type. An intraductal carcinoma component, non-comedo, comprised approximately 50% of the neoplasm, including the lactiferous ducts. Angiolymphatic involvement was present, and metastatic adenocarcinoma was present in 7 of 10 axillary lymph nodes. The largest nodal metastasis measured 3 cm, and focal extracapsular extension was identified. Family history included atherosclerotic coronary artery disease, type II diabetes, cerebrovascular disease, and depressive disorder.
BRSTTUT01	PSPORT1	Library was constructed using RNA isolated from breast tumor tissue removed from a 55-year-old Caucasian female during a unilateral extended simple mastectomy. Pathology indicated invasive grade 4 mammary adenocarcinoma of mixed lobular and ductal type, extensively involving the left breast. The tumor was identified in the deep dermis near the lactiferous ducts with extracapsular extension. Seven mid and low and five high axillary lymph nodes were positive for tumor. Proliferative fibrocystic changes were characterized by apocrine metaplasia, sclerosing adenosis, cyst formation, and ductal hyperplasia without atypia. Patient history included atrial tachycardia, blood in the stool, and a benign breast neoplasm. Family history included benign hypertension, atherosclerotic coronary artery disease, cerebrovascular disease, and depressive disorder.
CONUTUT01	pINCY	Library was constructed using RNA isolated from sigmoid mesentery tumor tissue obtained from a 61-year-old female during a total abdominal hysterectomy and bilateral salpingo-oophorectomy with regional lymph node excision. Pathology indicated a metastatic grade 4 malignant mixed müllerian tumor present in the sigmoid mesentery at two sites.
CORPNOT02	pINCY	Library was constructed using RNA isolated from diseased corpus callosum tissue removed from the brain of a 74-year-old Caucasian male who died from Alzheimer's disease.

Table 6

Library	Vector	Library Description
HEAANOT01	pINCY	Library was constructed using RNA isolated from right coronary and right circumflex coronary artery tissue removed from the explanted heart of a 46-year-old Caucasian male during a heart transplantation. Patient history included myocardial infarction from total occlusion of the left anterior descending coronary artery, atherosclerotic coronary artery disease, hyperlipidemia, myocardial ischemia, dilated cardiomyopathy, left ventricular dysfunction, and tobacco abuse. Previous surgeries included cardiac catheterization. Family history included atherosclerotic coronary artery disease.
HEARFET01	pINCY	Library was constructed using RNA isolated from heart tissue removed from a Hispanic male fetus, who died at 18 weeks' gestation.
KIDNFEC01	PBLUESCRIPT	Library was constructed using RNA isolated from kidney tissue removed from a pool of twelve Caucasian male and female fetuses that were spontaneously aborted at 19-23 weeks' gestation.
KIDNNOT09	pINCY	Library was constructed using RNA isolated from the kidney tissue of a Caucasian male fetus, who died at 23 weeks' gestation.
KIDNNOT20	pINCY	Library was constructed using RNA isolated from left kidney tissue removed from a 43-year-old Caucasian male during nephroureterectomy, regional lymph node excision, and unilateral left adrenalectomy. Pathology for the associated tumor tissue indicated a grade 2 renal cell carcinoma. Family history included atherosclerotic coronary artery disease.
LIVRNOT21	pINCY	Library was constructed using RNA isolated from liver tissue removed from a 29-year-old Caucasian male who died from massive head injury due to a motor vehicle accident. Serology was positive for cytomegalovirus.
LUNGDIN02	pINCY	This normalized lung tissue library was constructed from 7.6 million independent clones from a diseased lung tissue library. Starting RNA was made from RNA isolated from diseased lung tissue. Pathology indicated idiopathic pulmonary disease. The library was normalized in 2 rounds using conditions adapted from Soares et al., PNAS (1994) 91:9228-9232 and Bonaldo et al., Genome Research 6 (1996):791, except that a significantly longer (48 hours/round) reannealing hybridization was used.
LUNGNON03	PSPORT1	This normalized library was constructed from 2.56 million independent clones from a lung tissue library. RNA was made from lung tissue removed from the left lobe of a 58-year-old Caucasian male during a segmental lung resection. Pathology for the associated tumor tissue indicated a metastatic grade 3 (of 4) osteosarcoma. Patient history included soft tissue cancer, secondary cancer of the lung, prostate cancer, and an acute duodenal ulcer with hemorrhage. Patient also received radiation therapy to the retroperitoneum. Family history included prostate cancer, breast cancer, and acute leukemia. The normalization and hybridization conditions were adapted from Soares et al., PNAS (1994) 91:9228; Swaroop et al., NAR (1991) 19:1954; and Bonaldo et al., Genome Research (1996) 6:791.

Table 6

Library	Vector	Library Description
LUNGNOT35	pINCY	Library was constructed using RNA isolated from lung tissue removed from a 62-year-old Caucasian female. Pathology for the associated tumor tissue indicated a grade 1 spindle cell carcinoma forming a nodule. Patient history included depression, thrombophlebitis, and hyperlipidemia. Family history included cerebrovascular disease, atherosclerotic coronary artery disease, breast cancer, colon cancer, type II diabetes, and malignant skin melanoma.
MENITUT03	pINCY	Library was constructed using RNA isolated from brain meningioma tissue removed from a 35-year-old Caucasian female during excision of a cerebral meningeal lesion. Pathology indicated a benign neoplasm in the right cerebellopontine angle of the brain. Patient history included hypothyroidism. Family history included myocardial infarction and breast cancer.
MLP000032	PCR2-TOPO TA	Library was constructed using pooled cDNA from different donors. cDNA was generated using mRNA isolated from the following: aorta, cerebellum, lymph nodes, muscle, tonsil (lymphoid hyperplasia), bladder tumor (invasive grade 3 transitional cell carcinoma.), breast (proliferative fibrocystic changes without atypia characterized by epithelial ductal hyperplasia, testicle tumor (embryonal carcinoma), spleen, ovary, parathyroid, ileum, breast skin, sigmoid colon, penis tumor (fungating invasive grade 4 squamous cell carcinoma), fetal lung., breast, fetal small intestine, fetal liver, fetal pancreas, fetal lung, fetal skin, fetal penis, fetal bone, fetal ribs, frontal brain tumor (grade 4 gemistocytic astrocytoma), ovary (stromal hyperthecosis), bladder, bladder tumor (invasive grade 3 transitional cell carcinoma), stomach, lymph node tumor (metastatic basaloid squamous cell carcinoma), tonsil (reactive lymphoid hyperplasia), periosteum from the tibia, fetal brain, fetal spleen, uterus tumor, endometrial (grade 3 adenosquamous carcinoma), seminal vesicle, liver, aorta, adrenal gland, lymph node (metastatic grade 3 squamous cell carcinoma), glossal muscle, esophagus,
		esophagus tumor (invasive grade 3 adenocarcinoma), ileum, pancreas, soft tissue tumor from the skull (grade 3 ependymoma), transverse colon, (benign familial polyposis), rectum tumor (grade 3 colonic adenocarcinoma), rib tumor, (metastatic grade 3 osteosarcoma), lung, heart, placenta, thymus, stomach, spleen (splenomegaly with congestion), uterus, cervix (mild chronic cervicitis with focal squamous metaplasia), spleen tumor (malignant lymphoma, diffuse large cell type B-cell phenotype with abundant reactive T-cells and marked granulomatous response), umbilical cord blood mononuclear cells, upper lobe lung tumor, (grade 3 squamous cell carcinoma), endometrium (secretory phase), liver, liver tumor (metastatic grade 2 neuroendocrine carcinoma), colon, umbilical cord blood, Th1 cells, nonactivated, umbilical cord blood, Th2 cells, nonactivated, coronary artery endothelial cells (untreated), coronary artery smooth muscle cells, (untreated), coronary artery smooth muscle cells (treated with TNF & IL-1 10ng/ml each for 20 hours), bladder (mild chronic cystitis), epiglottitis, breast skin, small intestine, fetal prostate stroma fibroblasts, prostate epithelial cells (PTEC cells),

Table 6

Library	Vector	Library Description
MLP000032 (cont.)		<p>fetal adrenal glands, fetal liver, kidney transformed embryonal cell line (293-EBNA) (untreated), kidney transformed embryonal cell line (293-EBNA) (treated with 5Aza-2deoxycytidine for 72 hours), mammary epithelial cells, (HMEC cells), peripheral blood monocytes (treated with IL-10 at time 0, 10ng/ml, LPS was added at 1 hour at 5ng/ml. Incubation 24 hours), peripheral blood monocytes (treated with anti-IL-10 at time 0, 10ng/ml, LPS was added at 1 hour at 5ng/ml. Incubation 24 hours), spinal cord, base of medulla (Huntington's chorea), thigh and arm muscle (ALS), breast skin fibroblast (untreated), breast skin fibroblast (treated with 9CIS Retinoic Acid 1<math>\mu</math>M for 20 hours), breast skin fibroblast (treated with TNF-alpha &amp; IL-1 beta, 10ng/ml each for 20 hours), fetal liver mast cells, hematopoietic (Mast cells prepared from human fetal liver hematopoietic progenitor cells (CD34+ stem cells) cultured in the presence of hIL-6 and hSCF for 18 days), epithelial layer of colon, bronchial epithelial cells (treated for 20hours with 20% smoke conditioned media), lymph node, pooled peripheral blood mononuclear cells (untreated), pooled brain segments: striatum, globus</p>
		<p>pallidus and posterior putamen (Alzheimer's Disease), pituitary gland, umbilical cord blood, CD34+ derived dendritic cells (treated with SCF, GM-CSF &amp; TNF alpha, 13 days), umbilical cord blood, CD34+ derived dendritic cells (treated with SCF, GM-CSF &amp; TNF alpha, 13 days followed by PMA/Ionomycin for 5 hours), small intestine, rectum, bone marrow neuroblastoma cell line (SH-SY5Y cells, treated with 6-Hydroxydopamine 100 uM for 8 hours), bone marrow, neuroblastoma cell line (SH-SY5Y cells, untreated), brain segments from one donor: amygdala, entorhinal cortex, globus pallidus, substantia innominata, striatum, dorsal caudate nucleus, dorsal putamen, ventral nucleus accumbens, archaecortex (hippocampus anterior and posterior), thalamus, nucleus raphe magnus, periaqueductal gray, midbrain, substantia nigra, and dentate nucleus, pineal gland (Alzheimer's Disease), preadipocytes (untreated), preadipocytes (treated with a peroxisome proliferator-activated receptor gamma agonist, 1microm, 4 hours), pooled prostate (adenofibromatous hyperplasia), pooled kidney, pooled adipocytes (untreated), pooled adipocytes (treated with human insulin),</p>

Table 6

Library	Vector	Library Description
MLP000032 (cont.)		<p>pooled mesenteric and abdominal fat, pooled adrenal glands, pooled thyroid (normal and adenomatous hyperplasia), pooled spleen (normal and with changes consistent with idiopathic thrombocytopenic purpura), pooled right and left breast, pooled lung, pooled nasal polyps, pooled fat, pooled synovium (normal and rheumatoid arthritis), pooled brain (meningioma, gemistocytic astrocytoma, and Alzheimer's disease), pooled fetal colon, pooled colon: ascending, descending (chronic ulcerative colitis), and rectal tumor (adenocarcinoma), pooled esophagus, normal and tumor (invasive grade 3 adenocarcinoma), pooled breast skin fibroblast (one treated w/9CIS Retinoic Acid and the other with TNF-alpha &amp; IL-1 beta), pooled gallbladder (acute necrotizing cholecystitis with cholelithiasis (clinically hydrops), acute hemorrhagic cholecystitis with cholelithiasis, chronic cholecystitis and cholelithiasis), pooled fetal heart, (Patau's and fetal demise), pooled neurogenic tumor cell line, SK-N-MC, (neuroepithelioma, metastasis to supra-orbital area, untreated) and neuron, NT-2 cell line, (treated with mouse leptin at 1 <math>\mu</math>g/ml and 9cis retinoic acid at 3.3 <math>\mu</math>M</p>
		<p>for 6 days), pooled ovary (normal and polycystic ovarian disease), pooled prostate, (adenofibromatous hyperplasia), pooled seminal vesicle, pooled small intestine, pooled fetal small intestine, pooled stomach and fetal stomach, prostate epithelial cells, pooled testis (normal and embryonal carcinoma), pooled uterus, pooled uterus tumor (grade 3 adenosquamous carcinoma and leiomyoma), pooled uterus, endometrium, and myometrium, (normal and adenomatous hyperplasia with squamous metaplasia and focal atypia), pooled brain: (temporal lobe meningioma, cerebellum and hippocampus (Alzheimer's Disease), pooled skin, fetal lung, adrenal tumor (adrenal cortical carcinoma), prostate tumor (adenocarcinoma), fetal heart, fetal small intestine, ovary tumor (mucinous cystadenoma), ovary, ovary tumor (transitional cell carcinoma), disease prostate (adenofibromatous hyperplasia), fetal colon, uterus tumor (leiomyoma), temporal brain, submandibular gland, colon tumor (adenocarcinoma), ascending and transverse colon, ovary tumor (endometrioid carcinoma), lung tumor (squamous cell carcinoma), fetal brain, fetal lung, ureter tumor (transitional cell carcinoma),</p>



Table 6

Library	Vector	Library Description
MLP000032 (cont.)		untreated HNT cells, para-aortic soft tissue, testis, seminal vesicle, diseased ovary (endometriosis), temporal lobe, myometrium, diseased gallbladder (cholecystitis, cholelithiasis), placenta, breast tumor (ductal adenocarcinoma), breast, lung tumor (liposarcoma), endometrium, abdominal fat, cervical spine dorsal root ganglion, thoracic spine dorsal root ganglion, diseased thyroid (adenomatous hyperplasia), liver, kidney, fetal liver, NT-2 cells (treated with mouse leptin and 9cis RA), K562 cells (treated with 9cis RA), cerebellum, corpus callosum, hypothalamus, fetal brain astrocytes (treated with TNFa and IL-1b), inferior parietal cortex, posterior hippocampus, pons, thalamus, C3A cells (untreated), C3A cells (treated with 3-methylcholanthrene), testis, colon epithelial layer, pooled prostate, pooled liver, substantia nigra, thigh muscle, rib bone, fallopian tube tumor (endometrioid and serous adenocarcinoma), diseased lung (idiopathic pulmonary disease), cingulate anterior allocortex and neocortex, cingulate posterior allocortex, auditory neocortex, frontal neocortex, orbital inferior neocortex, parietal superior neocortex, visual primary neocortex, dentate nucleus, posterior cingulate,
		cerebellum, vermis, inferior temporal cortex, medulla, posterior parietal cortex, colon polyp, pooled breast, anterior and posterior hippocampus, mesenteric and abdominal fat, pooled esophagus, pooled fetal kidney, pooled fetal liver, ileum, small intestine, pooled gallbladder, frontal and superior temporal cortex, pooled ovary, pooled endometrium, pooled prostate, pooled kidney, fetal femur, sacrum tumor (giant cell tumor), pooled kidney and kidney tumor (renal cell carcinoma clear-cell type), pooled liver and liver tumor (neuroendocrine carcinoma), pooled fetal liver, pooled lung, fetal pancreas, pancreas, parotid gland, parotid tumor (sebaceous lymphadenoma), retroperitoneal and supraglottic soft tissue, spleen, fetal spleen, spleen tumor (malignant lymphoma), diseased spleen (idiopathic thrombocytopenic purpura), parathyroid, thyroid, thymus, tonsil ureter tumor (transitional cell carcinoma), pooled adrenal gland and adrenal tumor (pheochromocytoma), pooled lymph node tumor (Hodgkin's disease and metastatic adenocarcinoma), pooled neck and calf muscles, and pooled bladder
MONOTXT01	pINCY	Library was constructed using RNA isolated from treated monocytes from peripheral blood obtained from a 42-year-old female. The cells were treated with anti IL-10 and LPS.
NEUTFMT01	PBLUESCRIPT	Library was constructed using total RNA isolated from peripheral blood granulocytes collected by density gradient centrifugation through Ficoll-Hypaque. The cells were isolated from buffy coat units obtained from unrelated male and female donors. Cells were cultured in 10 nM fMLP for 30 minutes, lysed in GuSCN, and spun through CsCl to obtain RNA for library construction. Because this library was made from total RNA, it has an unusually high proportion of unique singleton sequences, which may not all come from polyA RNA species.

Table 6

Library	Vector	Library Description
OVARDIR01	PCDNA2.1	This random primed library was constructed using RNA isolated from right ovary tissue removed from a 45-year-old Caucasian female during total abdominal hysterectomy, bilateral salpingo-oophorectomy, vaginal suspension and fixation, and incidental appendectomy. Pathology indicated stromal hyperthecosis of the right and left ovaries. Pathology for the matched tumor tissue indicated a dermoid cyst (benign cystic teratoma) in the left ovary. Multiple (3) intramural leiomyomata were identified. The cervix showed squamous metaplasia. Patient history included metrorrhagia, female stress incontinence, alopecia, depressive disorder, pneumonia, normal delivery, and deficiency anemia. Family history included benign hypertension, atherosclerotic coronary artery disease, hyperlipidemia, and primary tuberculous complex.
PLACFEB01	pINCY	Library was constructed using pooled cDNA from two different donors. cDNA was generated using RNA isolated from placenta tissue removed from a Caucasian fetus (donor A), who died after 16 weeks' gestation from fetal demise and hydrocephalus; and a Caucasian male fetus (donor B), who died after 18 weeks' gestation from fetal demise. Patient history included umbilical cord wrapped around the head (3 times) and the shoulders (1 time) in donor A. Serology was positive for anti-CMV in donor A. Family history included multiple pregnancies and live births, and an abortion in donor A.
PLACNOT07	pINCY	Library was constructed using RNA isolated from placental tissue removed from a Caucasian fetus, who died after 16 weeks' gestation from fetal demise and hydrocephalus. Serology was positive for anti-CMV (cytomegalovirus).
PROSBPS05	pINCY	This subtraced prostate tissue library was constructed using 4.48x10 <sup>5</sup> clones from diseased prostate tissue and was subjected to two rounds of subtraction hybridization with 1.56 million clones from a breast tissue library. The starting library for subtraction was constructed using RNA isolated from diseased prostate tissue removed from a 70-year-old Caucasian male during a radical prostatectomy and closed prostatic biopsy. Pathology indicated benign prostatic hypertrophy. Pathology for the matched tumor tissue indicated adenocarcinoma. The patient presented with elevated prostate specific antigen and induration. Patient history included benign hypertension, gastrointestinal bleed, cardiac dysrhythmia, cardiac arrest, hyperlipidemia, alcohol abuse and fractured mandible. Previous surgeries included splenectomy, cholecystectomy and inguinal hernia repair. Patient medications included Verapamil and antacids. Family history included benign hypertension, myocardial infarction and coronary atherosclerosis in the mother; tobacco abuse and lung cancer in the father; tobacco abuse, cerebrovascular accident and lung cancer in the sibling(s). The
		hybridization probe for subtraction was derived from a similarly constructed library from RNA isolated from nontumorous breast tissue from a different donor. Subtractive hybridization conditions were based on the methodologies of Swaroop et al., NAR 19 (1991):1954 and Donaldo, et al. Genome Research 6 (1996): 791.

Table 6

Library	Vector	Library Description
PROSNON01	PSPORT1	This normalized prostate library was constructed from 4.4 M independent clones from a prostate library. Starting RNA was made from prostate tissue removed from a 28-year-old Caucasian male who died from a self-inflicted gunshot wound. The normalization and hybridization conditions were adapted from Soares, M.B. et al. (1994) Proc. Natl. Acad. Sci. USA 91:9228-9232, using a longer (19 hour) reannealing hybridization period.
PROSNOT19	pINCY	Library was constructed using RNA isolated from diseased prostate tissue removed from a 59-year-old Caucasian male during a radical prostatectomy with regional lymph node excision. Pathology indicated adenofibromatous hyperplasia. Pathology for the associated tumor tissue indicated an adenocarcinoma (Gleason grade 3+3). The patient presented with elevated prostate-specific antigen (PSA). Patient history included colon diverticuli, asbestosis, and thrombophlebitis. Previous surgeries included a partial colectomy. Family history included benign hypertension, multiple myeloma, hyperlipidemia and rheumatoid arthritis.
PROSTUS23	pINCY	This subtracted prostate tumor library was constructed using 10 million clones from a pooled prostate tumor library that was subjected to 2 rounds of subtractive hybridization with 10 million clones from a pooled prostate tissue library. The starting library for subtraction was constructed by pooling equal numbers of clones from 4 prostate tumor libraries using mRNA isolated from prostate tumor removed from Caucasian males at ages 58 (A), 61 (B), 66 (C), and 68 (D) during prostatectomy with lymph node excision. Pathology indicated adenocarcinoma in all donors. History included elevated PSA, induration and tobacco abuse in donor A; elevated PSA, induration, prostate hyperplasia, renal failure, osteoarthritis, renal artery stenosis, benign HTN, thrombocytopenia, hyperlipidemia, tobacco/alcohol abuse and hepatitis C (carrier) in donor B; elevated PSA, induration, and tobacco abuse in donor C; and elevated PSA, induration, hypercholesterolemia, and kidney calculus in donor D. The hybridization probe for subtraction was constructed by pooling equal numbers of cDNA clones from 3 prostate tissue libraries derived from prostate tissue, prostate epithelial cells,
		and fibroblasts from prostate stroma from 3 different donors. Subtractive hybridization conditions were based on the methodologies of Swaroop et al., NAR 19 (1991):1954 and Bonaldo, et al. Genome Research 6 (1996):791.
PROSTUT05	PSPORT1	Library was constructed using RNA isolated from prostate tumor tissue removed from a 69-year-old Caucasian male during a radical prostatectomy. Pathology indicated adenocarcinoma (Gleason grade 3+4). Adenofibromatous hyperplasia was also present. Family history included congestive heart failure, multiple myeloma, hyperlipidemia, and rheumatoid arthritis.
SINTNOT18	pINCY	Library was constructed using RNA isolated from small intestine tissue obtained from a 59-year-old male.

Table 6

Library	Vector	Library Description
STOMTDE01	PCDNA2.1	This 5' biased random primed library was constructed using RNA isolated from stomach tissue removed from a 61-year-old Caucasian male during a partial esophagectomy, proximal gastrectomy, pyloromyotomy, and regional lymph node excision. Pathology for the associated tumor indicated an invasive grade 3 adenocarcinoma in the esophagus, extending distally to involve the gastroesophageal junction. The tumor extended through the muscularis to involve periesophageal and perigastric soft tissues. One perigastric and two periesophageal lymph nodes were positive for tumor. There were multiple perigastric and periesophageal tumor implants. The patient presented with deficiency anemia and myelodysplasia. Patient history included hyperlipidemia, and tobacco and alcohol abuse in remission. Previous surgeries included adenotomysilectomy, rhinoplasty, vasectomy, and hemorrhoidectomy. A previous bone marrow aspiration found the marrow to be hypercellular for age and had a cellularity-to-fat ratio of 95:5. The marrow was focally densely fibrotic. Granulocytic precursors were slightly increased with normal maturation. The estimate of blast cells was greater than 5%.
		Megakaryocytes were increased and appeared atypical in clusters. Storage cells and granulomata were absent. Patient medications included Epoetin, Danocrine, Berocea Plus tablets, Selenium, vitamin B6 phosphate, vitamins E & C, and beta carotene. Family history included alcohol abuse, atherosclerotic coronary artery disease, type II diabetes, chronic liver disease, and primary cardiomyopathy in the father; and benign hypertension and cerebrovascular disease in the mother.
TESTNOT03	PBLUESCRIPT	Library was constructed using RNA isolated from testicular tissue removed from a 37-year-old Caucasian male, who died from liver disease. Patient history included cirrhosis, jaundice, and liver failure.
TESTTUT02	pINCY	Library was constructed using RNA isolated from testicular tumor removed from a 31-year-old Caucasian male during unilateral orchiectomy. Pathology indicated embryonal carcinoma.
THYMNOE02	PCDNA2.1	This 5' biased random primed library was constructed using RNA isolated from thymus tissue removed from a 3-year-old Hispanic male during a thymectomy and closure of a patent ductus arteriosus. The patient presented with severe pulmonary stenosis and cyanosis. Patient history included a cardiac catheterization and echocardiogram. Previous surgeries included Blalock-Taussig shunt and pulmonary valvotomy. The patient was not taking any medications. Family history included benign hypertension, osteoarthritis, depressive disorder, and extrinsic asthma in the grandparent(s).

Table 6

Library	Vector	Library Description
THYMNOT05	pINCY	Library was constructed using RNA isolated from thymus tissue removed from a 3-year-old Hispanic male during a thymectomy and closure of a patent ductus arteriosus. The patient presented with severe pulmonary stenosis and cyanosis. Patient history included a cardiac catheterization and echocardiogram. Previous surgeries included Blalock-Taussig shunt and pulmonary valvotomy. The patient was not taking any medications. Family history included benign hypertension, osteoarthritis, depressive disorder, and extrinsic asthma in the grandparent(s).
THYRTUT03	pINCY	Library was constructed using RNA isolated from benign thyroid tumor tissue removed from a 17-year-old Caucasian male during a thyroidectomy. Pathology indicated encapsulated follicular adenoma forming a circumscribed mass.
TLYMUNT01	pINCY	Library was constructed using RNA isolated from resting allogenic T-lymphocyte tissue removed from an adult (40-50-year old) Caucasian male.
TONSDIC01	PSPORT1	This large size fractionated library was constructed using pooled cDNA from two donors. cDNA was generated using mRNA isolated from diseased left tonsil tissue removed from a 6-year-old Caucasian male (donor A) during adenotonsillectomy and from diseased right tonsil tissue removed from a 9-year-old Caucasian female (donor B) during adenotonsillectomy. Pathology indicated reactive lymphoid hyperplasia, bilaterally (A) and lymphoid hyperplasia (B). The patients presented with sleep apnea (A) and hypertrophy of tonsils, cough, and unspecified nasal and sinus disease (B). Patient history included a bacterial infection (A). Previous surgeries included myringotomy with tube insertion (A). Donor A was not taking any medications and donor B was taking Vancenase. Family history included benign hypertension, myocardial infarction, and atherosclerotic coronary artery disease in the grandparent(s) of donor A; and extrinsic asthma and unspecified allergy in the mother; unspecified allergy in the father; benign hypertension, deficiency anemia, osteoarthritis, extrinsic asthma and unspecified allergy in the grandparent(s) of donor B.
UTRSTMR01	pINCY	Library was constructed using RNA isolated from uterine myometrial tissue removed from a 41-year-old Caucasian female during a vaginal hysterectomy. The endometrium was secretory and contained fragments of endometrial polyps. Pathology for associated tumor tissue indicated uterine leiomyoma. Patient history included ventral hernia and a benign ovarian neoplasm.

Table 6

Library	Vector	Library Description
UTRSTUE01	PCDNA2.1	This 5' biased random primed library was constructed using RNA isolated from uterus tumor tissue removed a 37-year-old Black female during myomectomy, dilation and curettage, right fimbrial region biopsy, and incidental appendectomy. Pathology indicated multiple (12) uterine leiomyomata. A fimbrial cyst was identified. The patient presented with deficiency anemia, an umbilical hernia, and premenopausal menorrhagia. Patient history included premenopausal menorrhagia and sarcoidosis of the lung. Previous surgeries included hysterectomy, dilation and curettage, and an endoscopic lung biopsy. Patient medications included Chromagen and Claritin. Family history included acute myocardial infarction and atherosclerotic coronary artery disease in the father.

Table 7

Program	Description	Reference	Parameter Threshold
ABI FACTURA	A program that removes vector sequences and masks ambiguous bases in nucleic acid sequences.	Applied Biosystems, Foster City, CA.	
ABI/PARACEL FDF	A Fast Data Finder useful in comparing and annotating amino acid or nucleic acid sequences.	Applied Biosystems, Foster City, CA; Paracel Inc., Pasadena, CA.	Mismatch <50%
ABI AutoAssembler	A program that assembles nucleic acid sequences.	Applied Biosystems, Foster City, CA.	
BLAST	A Basic Local Alignment Search Tool useful in sequence similarity search for amino acid and nucleic acid sequences. BLAST includes five functions: blastp, blastn, blastx, tblastn, and tblastx.	Altschul, S.F. et al. (1990) J. Mol. Biol. 215:403-410; Altschul, S.F. et al. (1997) Nucleic Acids Res. 25:3389-3402.	ESTs: Probability value=1.0E-8 or less Full Length sequences: Probability value= 1.0E-10 or less
FASTA	A Pearson and Lipman algorithm that searches for similarity between a query sequence and a group of sequences of the same type. FASTA comprises at least five functions: fasta, tfasta, fastx, tfastx, and ssearch.	Pearson, W.R. and D.J. Lipman (1988) Proc. Natl. Acad. Sci. USA 85:2444-2448; Pearson, W.R. (1990) Methods Enzymol. 183:63-98; and Smith, T.F. and M.S. Waterman (1981) Adv. Appl. Math. 2:482-489.	ESTs: fasta E value=1.06E-6 Assembled ESTs: fasta Identity= 95% or greater and Match length=200 bases or greater; fastx E value=1.0E-8 or less Full Length sequences: fastx score=100 or greater
BLIMPS	A BLocks IMProved Searcher that matches a sequence against those in BLOCKS, PRINTS, DOMO, PRODOM, and PFAM databases to search for gene families, sequence homology, and structural fingerprint regions.	Henikoff, S. and J.G. Henikoff (1991) Nucleic Acids Res. 19:6565-6572; Henikoff, J.G. and S. Henikoff (1996) Methods Enzymol. 266:88-105; and Attwood, T.K. et al. (1997) J. Chem. Inf. Comput. Sci. 37:417-424.	Probability value=1.0E-3 or less
HMMER	An algorithm for searching a query sequence against hidden Markov model (HMM)-based databases of protein family consensus sequences, such as PFAM, INCY, SMART, and TIGRFAM.	Krogh, A. et al. (1994) J. Mol. Biol. 235:1501-1531; Sonnhammer, E.L.L. et al. (1998) Nucleic Acids Res. 26:320-322; Durbin, R. et al. (1998) Our World View, in a Nutshell, Cambridge Univ. Press, pp. 1-350.	PFAM, INCY, SMART, or TIGRFAM hits: Probability value=1.0E-3 or less Signal peptide hits: Score= 0 or greater

Table 7 (cont.)

Program	Description	Reference	Parameter Threshold
ProfileScan	An algorithm that searches for structural and sequence motifs in protein sequences that match sequence patterns defined in Prosite.	Gribskov, M. et al. (1988) CABIOS 4:61-66; Gribskov, M. et al. (1989) Methods Enzymol. 183:146-159; Bairoch, A. et al. (1997) Nucleic Acids Res. 25:217-221.	Normalized quality score > GCG-specified "HIGH" value for that particular Prosite motif. Generally, score=1.4-2.1.
Phred	A base-calling algorithm that examines automated sequencer traces with high sensitivity and probability.	Ewing, B. et al. (1998) Genome Res. 8:175-185; Ewing, B. and P. Green (1998) Genome Res. 8:186-194.	
Phrap	A Phils Revised Assembly Program including SWAT and CrossMatch, programs based on efficient implementation of the Smith-Waterman algorithm, useful in searching sequence homology and assembling DNA sequences.	Smith, T.F. and M.S. Waterman (1981) Adv. Appl. Math. 2:482-489; Smith, T.F. and M.S. Waterman (1981) J. Mol. Biol. 147:195-197; and Green, P., University of Washington, Seattle, WA.	Score=120 or greater; Match length=56 or greater
Consed	A graphical tool for viewing and editing Phrap assemblies.	Gordon, D. et al. (1998) Genome Res. 8:195-202.	
SPScan	A weight matrix analysis program that scans protein sequences for the presence of secretory signal peptides.	Nielson, H. et al. (1997) Protein Engineering 10:1-6; Claverie, J.M. and S. Audic (1997) CABIOS 12:431-439.	Score=3.5 or greater
TMAP	A program that uses weight matrices to delineate transmembrane segments on protein sequences and determine orientation.	Persson, B. and P. Argos (1994) J. Mol. Biol. 237:182-192; Persson, B. and P. Argos (1996) Protein Sci. 5:363-371.	
TMHMMER	A program that uses a hidden Markov model (HMM) to delineate transmembrane segments on protein sequences and determine orientation.	Sonnhammer, E.L. et al. (1998) Proc. Sixth Intl. Conf. on Intelligent Systems for Mol. Biol., Glasgow et al., eds., The Am. Assoc. for Artificial Intelligence Press, Menlo Park, CA, pp. 175-182.	
Motifs	A program that searches amino acid sequences for patterns that matched those defined in Prosite.	Bairoch, A. et al. (1997) Nucleic Acids Res. 25:217-221; Wisconsin Package Program Manual, version 9, page M51-59, Genetics Computer Group, Madison, WI.	



Table 8

SEQ ID NO:	PID	EST ID	SNP ID	EST SNP	CB1 SNP	EST Allele	Allele 1	Allele 2	Amino Acid	Caucasian Allele 1 frequency	African Allele 1 frequency	Asian Allele 1 frequency	Hispanic Allele 1 frequency
112	7503849	1339126H1	SNP00112738	151	315	A	G	A	T80	n/a	n/a	n/a	n/a
112	7503849	1376303H1	SNP00009519	85	38	C	C	A	noncoding	n/a	n/a	n/a	n/a
112	7503849	1376303H1	SNP00037704	88	35	G	G	A	noncoding	n/a	n/a	n/a	n/a
112	7503849	1422323H1	SNP00061236	167	384	T	C	T	stop103	n/d	n/d	n/d	n/d
112	7503849	1520683H1	SNP00009519	131	39	C	C	A	noncoding	n/a	n/a	n/a	n/a
112	7503849	1520683H1	SNP00037704	134	36	G	G	A	noncoding	n/a	n/a	n/a	n/a
112	7503849	2211818H1	SNP00097061	219	1021	C	C	T	noncoding	n/a	n/a	n/a	n/a
112	7503849	2346103H1	SNP00037704	106	27	G	G	A	noncoding	n/a	n/a	n/a	n/a
112	7503849	2497486H1	SNP00009519	84	41	C	C	A	noncoding	n/a	n/a	n/a	n/a
112	7503849	2497486H1	SNP00037704	87	38	G	G	A	noncoding	n/a	n/a	n/a	n/a
112	7503849	2688333H1	SNP00009519	103	42	C	C	A	noncoding	n/a	n/a	n/a	n/a
112	7503849	2688333H1	SNP00037704	106	39	G	G	A	noncoding	n/a	n/a	n/a	n/a
112	7503849	2691537H1	SNP00009519	228	106	G	G	T	R10	n/a	n/a	n/a	n/a
112	7503849	2691537H1	SNP00037704	225	109	C	C	T	P11	n/a	n/a	n/a	n/a
112	7503849	2984764H1	SNP00037704	84	100	C	C	T	P8	n/a	n/a	n/a	n/a
112	7503849	2998532H1	SNP00092683	42	1103	C	C	T	noncoding	n/a	n/a	n/a	n/a
112	7503849	3083817H1	SNP00092683	97	1102	T	C	T	noncoding	n/a	n/a	n/a	n/a
112	7503849	3083817H1	SNP00097061	15	1020	C	C	T	noncoding	n/a	n/a	n/a	n/a
112	7503849	3163442H1	SNP00097061	252	1015	C	C	T	noncoding	n/a	n/a	n/a	n/a
112	7503849	3184509H1	SNP00009519	79	94	G	G	T	G6	n/a	n/a	n/a	n/a
112	7503849	3184509H1	SNP00037704	82	97	C	C	T	P7	n/a	n/a	n/a	n/a
112	7503849	3184509H1	SNP00112738	288	305	G	G	A	S76	n/a	n/a	n/a	n/a
112	7503849	3319727H1	SNP00092683	71	1101	C	C	T	noncoding	n/a	n/a	n/a	n/a
112	7503849	3360460H1	SNP00009519	85	44	C	C	A	noncoding	n/a	n/a	n/a	n/a
112	7503849	3501445H1	SNP00009519	97	102	T	G	T	C9	n/a	n/a	n/a	n/a
112	7503849	3692522H1	SNP00061236	202	381	C	C	T	P102	n/d	n/d	n/d	n/d
112	7503849	3748594H1	SNP00112738	84	313	A	G	A	H79	n/a	n/a	n/a	n/a
112	7503849	3777748H1	SNP00112738	239	291	G	G	A	G72	n/a	n/a	n/a	n/a

Table 8

SEQ ID NO:	PID	EST ID	SNP ID	EST SNP	CB1 SNP	EST Allele	Allele 1	Allele 2	Amino Acid	Caucasian Allele 1 frequency	African Allele 1 frequency	Asian Allele 1 frequency	Hispanic Allele 1 frequency
112	7503849	3877579H1	SNP00009519	47	96	T	G	T	S7	n/a	n/a	n/a	n/a
112	7503849	4205658H1	SNP000061236	49	382	C	C	T	A102	n/d	n/d	n/d	n/d
112	7503849	4541534H1	SNP00112739	225	609	C	C	T	H178	n/d	n/d	n/d	n/d
112	7503849	4575407H1	SNP000092683	54	1100	C	C	T	noncoding	n/a	n/a	n/a	n/a
112	7503849	4640189H1	SNP00112739	206	611	C	C	T	Y178	n/d	n/d	n/d	n/d
112	7503849	4916293H1	SNP000092683	43	1099	C	C	T	noncoding	n/a	n/a	n/a	n/a
112	7503849	4956713H1	SNP000097061	8	1019	C	C	T	noncoding	n/a	n/a	n/a	n/a
112	7503849	5026038H1	SNP00112739	75	602	C	C	T	R175	n/d	n/d	n/d	n/d
112	7503849	5206042H1	SNP000097061	135	851	C	C	T	noncoding	n/a	n/a	n/a	n/a
112	7503849	5872016H1	SNP000061236	159	375	C	C	T	L100	n/d	n/d	n/d	n/d
112	7503849	6732363H1	SNP00112740	410	627	C	C	T	L184	n/a	n/a	n/a	n/a

What is claimed is:

1. An isolated polypeptide selected from the group consisting of:

- 5 a) a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:1-55,
- b) a polypeptide consisting essentially of the amino acid sequence of SEQ ID NO:56,
- c) a polypeptide comprising a naturally occurring amino acid sequence at least 90% identical to an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:7-12, SEQ ID NO:14-20, SEQ ID NO:23-24, SEQ ID NO:26-36, SEQ ID NO:38-43, SEQ ID NO:45-46 and SEQ ID NO:48-54,
- 10 d) a polypeptide comprising a naturally occurring amino acid sequence at least 93% identical to the amino acid sequence of SEQ ID NO:37,
- e) a polypeptide comprising a naturally occurring amino acid sequence at least 94% identical to an amino acid sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:22 and SEQ ID NO:55,
- 15 f) a polypeptide comprising a naturally occurring amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO:13,
- g) a polypeptide comprising a naturally occurring amino acid sequence at least 97% identical to an amino acid sequence selected from the group consisting of SEQ ID NO:6 and SEQ ID NO:44,
- 20 h) a polypeptide comprising a naturally occurring amino acid sequence at least 98% identical to an amino acid sequence selected from the group consisting of SEQ ID NO:5, SEQ ID NO:21 and SEQ ID NO:25,
- i) a polypeptide comprising a naturally occurring amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO:1,
- 25 j) a biologically active fragment of a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1-56, and
- k) an immunogenic fragment of a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1-56.
- 30

2. An isolated polypeptide of claim 1 selected from the group consisting of:

- a) a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:1-55 and
- 35 b) a polypeptide consisting essentially of the amino acid sequence of SEQ ID NO:56.

3. An isolated polynucleotide encoding a polypeptide of claim 1.
4. An isolated polynucleotide encoding a polypeptide of claim 2.
- 5 5. An isolated polynucleotide of claim 4 comprising a polynucleotide sequence selected from the group consisting of SEQ ID NO:57-112.
6. A recombinant polynucleotide comprising a promoter sequence operably linked to a polynucleotide of claim 3.
- 10 7. A cell transformed with a recombinant polynucleotide of claim 6.
8. A transgenic organism comprising a recombinant polynucleotide of claim 6.
- 15 9. A method of producing a polypeptide of claim 1, the method comprising:
  - a) culturing a cell under conditions suitable for expression of the polypeptide, wherein said cell is transformed with a recombinant polynucleotide, and said recombinant polynucleotide comprises a promoter sequence operably linked to a polynucleotide encoding the polypeptide of claim 1, and
  - 20 b) recovering the polypeptide so expressed.
10. A method of claim 9, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of SEQ ID NO:1-56.
- 25 11. An isolated antibody which specifically binds to a polypeptide of claim 1.
12. An isolated polynucleotide selected from the group consisting of:
  - a) a polynucleotide comprising a polynucleotide sequence selected from the group consisting of SEQ ID NO:57-112,
  - 30 b) a polynucleotide comprising a naturally occurring polynucleotide sequence at least 90% identical to a polynucleotide sequence selected from the group consisting of SEQ ID NO:57-112,
  - c) a polynucleotide complementary to a polynucleotide of a),
  - d) a polynucleotide complementary to a polynucleotide of b), and
  - 35 e) an RNA equivalent of a)-d).

13. An isolated polynucleotide comprising at least 60 contiguous nucleotides of a polynucleotide of claim 12.

14. A method of detecting a target polynucleotide in a sample, said target polynucleotide  
5 having a sequence of a polynucleotide of claim 12, the method comprising:  
a) hybridizing the sample with a probe comprising at least 20 contiguous nucleotides  
comprising a sequence complementary to said target polynucleotide in the sample,  
and which probe specifically hybridizes to said target polynucleotide, under  
conditions whereby a hybridization complex is formed between said probe and said  
10 target polynucleotide or fragments thereof, and  
b) detecting the presence or absence of said hybridization complex, and, optionally, if  
present, the amount thereof.

15. A method of claim 14, wherein the probe comprises at least 60 contiguous nucleotides.

16. A method of detecting a target polynucleotide in a sample, said target polynucleotide  
having a sequence of a polynucleotide of claim 12, the method comprising:  
a) amplifying said target polynucleotide or fragment thereof using polymerase chain  
reaction amplification, and  
20 b) detecting the presence or absence of said amplified target polynucleotide or fragment  
thereof, and, optionally, if present, the amount thereof.

17. A composition comprising a polypeptide of claim 1 and a pharmaceutically acceptable  
excipient.

25 18. A composition of claim 17, wherein the polypeptide is selected from the group consisting  
of:  
a) a polypeptide comprising an amino acid sequence selected from the group consisting  
of SEQ ID NO:1-55, and  
30 b) a polypeptide consisting essentially of the amino acid sequence of SEQ ID NO:56.

19. A method for treating a disease or condition associated with decreased expression of  
functional MDDT, comprising administering to a patient in need of such treatment the composition of  
claim 17.

35

20. A method of screening a compound for effectiveness as an agonist of a polypeptide of claim 1, the method comprising:

- a) exposing a sample comprising a polypeptide of claim 1 to a compound, and
- b) detecting agonist activity in the sample.

5

21. A composition comprising an agonist compound identified by a method of claim 20 and a pharmaceutically acceptable excipient.

22. A method for treating a disease or condition associated with decreased expression of functional MDDT, comprising administering to a patient in need of such treatment a composition of claim 21.

23. A method of screening a compound for effectiveness as an antagonist of a polypeptide of claim 1, the method comprising:

- a) exposing a sample comprising a polypeptide of claim 1 to a compound, and
- b) detecting antagonist activity in the sample.

15

24. A composition comprising an antagonist compound identified by a method of claim 23 and a pharmaceutically acceptable excipient.

20

25. A method for treating a disease or condition associated with overexpression of functional MDDT, comprising administering to a patient in need of such treatment a composition of claim 24.

26. A method of screening for a compound that specifically binds to the polypeptide of claim 1, the method comprising:

25

- a) combining the polypeptide of claim 1 with at least one test compound under suitable conditions, and
- b) detecting binding of the polypeptide of claim 1 to the test compound, thereby identifying a compound that specifically binds to the polypeptide of claim 1.

30

27. A method of screening for a compound that modulates the activity of the polypeptide of claim 1, the method comprising:

- a) combining the polypeptide of claim 1 with at least one test compound under conditions permissive for the activity of the polypeptide of claim 1,
- b) assessing the activity of the polypeptide of claim 1 in the presence of the test

35

compound, and

- 5 c) comparing the activity of the polypeptide of claim 1 in the presence of the test compound with the activity of the polypeptide of claim 1 in the absence of the test compound, wherein a change in the activity of the polypeptide of claim 1 in the presence of the test compound is indicative of a compound that modulates the activity of the polypeptide of claim 1.

28. A method of screening a compound for effectiveness in altering expression of a target polynucleotide, wherein said target polynucleotide comprises a sequence of claim 5, the method comprising:

- 10 a) exposing a sample comprising the target polynucleotide to a compound, under conditions suitable for the expression of the target polynucleotide,  
b) detecting altered expression of the target polynucleotide, and  
c) comparing the expression of the target polynucleotide in the presence of varying  
15 amounts of the compound and in the absence of the compound.

29. A method of assessing toxicity of a test compound, the method comprising:

- 20 a) treating a biological sample containing nucleic acids with the test compound,  
b) hybridizing the nucleic acids of the treated biological sample with a probe comprising at least 20 contiguous nucleotides of a polynucleotide of claim 12 under conditions whereby a specific hybridization complex is formed between said probe and a target polynucleotide in the biological sample, said target polynucleotide comprising a polynucleotide sequence of a polynucleotide of claim 12 or fragment thereof,  
c) quantifying the amount of hybridization complex, and  
25 d) comparing the amount of hybridization complex in the treated biological sample with the amount of hybridization complex in an untreated biological sample, wherein a difference in the amount of hybridization complex in the treated biological sample is indicative of toxicity of the test compound.

30. A diagnostic test for a condition or disease associated with the expression of MDDT in a biological sample, the method comprising:

- 35 a) combining the biological sample with an antibody of claim 11, under conditions suitable for the antibody to bind the polypeptide and form an antibody:polypeptide complex, and  
b) detecting the complex, wherein the presence of the complex correlates with the

presence of the polypeptide in the biological sample.

31. The antibody of claim 11, wherein the antibody is:

- a) a chimeric antibody,
- b) a single chain antibody,
- c) a Fab fragment,
- d) a F(ab')<sub>2</sub> fragment, or
- e) a humanized antibody.

32. A composition comprising an antibody of claim 11 and an acceptable excipient.

33. A method of diagnosing a condition or disease associated with the expression of MDDT in a subject, comprising administering to said subject an effective amount of the composition of claim 32.

34. A composition of claim 32, wherein the antibody is labeled.

35. A method of diagnosing a condition or disease associated with the expression of MDDT in a subject, comprising administering to said subject an effective amount of the composition of claim 34.

36. A method of preparing a polyclonal antibody with the specificity of the antibody of claim 11, the method comprising:

- a) immunizing an animal with a polypeptide consisting of an amino acid sequence selected from the group consisting of SEQ ID NO:1-56, or an immunogenic fragment thereof, under conditions to elicit an antibody response,
- b) isolating antibodies from the animal, and
- c) screening the isolated antibodies with the polypeptide, thereby identifying a polyclonal antibody which specifically binds to a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:1-56.

37. A polyclonal antibody produced by a method of claim 36.

38. A composition comprising the polyclonal antibody of claim 37 and a suitable carrier.



39. A method of making a monoclonal antibody with the specificity of the antibody of claim 11, the method comprising:

- 5 a) immunizing an animal with a polypeptide consisting of an amino acid sequence selected from the group consisting of SEQ ID NO:1-56, or an immunogenic fragment thereof, under conditions to elicit an antibody response,
- b) isolating antibody producing cells from the animal,
- c) fusing the antibody producing cells with immortalized cells to form monoclonal antibody-producing hybridoma cells,
- d) culturing the hybridoma cells, and
- 10 e) isolating from the culture monoclonal antibody which specifically binds to a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:1-56.

40. A monoclonal antibody produced by a method of claim 39.

15

41. A composition comprising the monoclonal antibody of claim 40 and a suitable carrier.

42. The antibody of claim 11, wherein the antibody is produced by screening a Fab expression library.

20

43. The antibody of claim 11, wherein the antibody is produced by screening a recombinant immunoglobulin library.

44. A method of detecting a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:1-56 in a sample, the method comprising:

- 25 a) incubating the antibody of claim 11 with a sample under conditions to allow specific binding of the antibody and the polypeptide, and
- b) detecting specific binding, wherein specific binding indicates the presence of a polypeptide comprising an amino acid sequence selected from the group consisting of
- 30 SEQ ID NO:1-56 in the sample.

45. A method of purifying a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:1-56 from a sample, the method comprising:

- 35 a) incubating the antibody of claim 11 with a sample under conditions to allow specific binding of the antibody and the polypeptide, and

- b) separating the antibody from the sample and obtaining the purified polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:1-56.

5           46. A microarray wherein at least one element of the microarray is a polynucleotide of claim  
13.

47. A method of generating an expression profile of a sample which contains polynucleotides, the method comprising:

- 10           a) labeling the polynucleotides of the sample,  
            b) contacting the elements of the microarray of claim 46 with the labeled polynucleotides of the sample under conditions suitable for the formation of a hybridization complex, and  
            c) quantifying the expression of the polynucleotides in the sample.

15

48. An array comprising different nucleotide molecules affixed in distinct physical locations on a solid substrate, wherein at least one of said nucleotide molecules comprises a first oligonucleotide or polynucleotide sequence specifically hybridizable with at least 30 contiguous nucleotides of a target polynucleotide, and wherein said target polynucleotide is a polynucleotide of  
20 claim 12.

49. An array of claim 48, wherein said first oligonucleotide or polynucleotide sequence is completely complementary to at least 30 contiguous nucleotides of said target polynucleotide.

25           50. An array of claim 48, wherein said first oligonucleotide or polynucleotide sequence is completely complementary to at least 60 contiguous nucleotides of said target polynucleotide.

51. An array of claim 48, wherein said first oligonucleotide or polynucleotide sequence is completely complementary to said target polynucleotide.

30

52. An array of claim 48, which is a microarray.

53. An array of claim 48, further comprising said target polynucleotide hybridized to a nucleotide molecule comprising said first oligonucleotide or polynucleotide sequence.

35

54. An array of claim 48, wherein a linker joins at least one of said nucleotide molecules to said solid substrate.

55. An array of claim 48, wherein each distinct physical location on the substrate contains multiple nucleotide molecules, and the multiple nucleotide molecules at any single distinct physical location have the same sequence, and each distinct physical location on the substrate contains nucleotide molecules having a sequence which differs from the sequence of nucleotide molecules at another distinct physical location on the substrate.

56. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:1.

57. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:2.

58. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:3.

59. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:4.

60. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:5.

61. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:6.

62. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:7.

63. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:8.

64. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:9.

65. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:10.

66. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:11.

67. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:12.

68. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:13.

69. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:14.
70. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:15.
- 5 71. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:16.
72. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:17.
73. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:18.
- 10 74. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:19.
75. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:20.
- 15 76. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:21.
77. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:22.
78. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:23.
- 20 79. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:24.
80. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:25.
- 25 81. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:26.
82. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:27.
83. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:28.
- 30 84. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:29.
85. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:30.
- 35 86. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:31.

87. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:32.
88. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:33.
- 5 89. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:34.
90. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:35.
91. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:36.
- 10 92. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:37.
93. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:38.
- 15 94. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:39.
95. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:40.
96. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:41.
- 20 97. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:42.
98. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:43.
- 25 99. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:44.
100. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:45.
101. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:46.
- 30 102. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:47.
103. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:48.
- 35 104. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:49.

105. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:50.
106. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:51.
- 5 107. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:52.
108. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:53.
109. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:54.
- 10 110. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:55.
111. A polypeptide of claim 1, consisting essentially of the amino acid sequence of SEQ ID  
NO:56.
- 15 112. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
NO:57.
113. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
20 NO:58.
114. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
NO:59.
- 25 115. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
NO:60.
116. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
NO:61.
- 30 117. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
NO:62.
118. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
35 NO:63.

119. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
NO:64.

120. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
5 NO:65.

121. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
NO:66.

122. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
10 NO:67.

123. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
NO:68.

124. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
15 NO:69.

125. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
20 NO:70.

126. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
NO:71.

127. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
25 NO:72.

128. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
NO:73.

129. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
30 NO:74.

130. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
35 NO:75.

131. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
NO:76.

5 132. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
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133. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
NO:78.

10 134. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
NO:79.

135. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
NO:80.

15 136. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
NO:81.

20 137. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
NO:82.

138. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
NO:83.

25 139. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
NO:84.

140. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
NO:85.

30 141. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
NO:86.

35 142. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
NO:87.



143. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
NO:88.

144. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
5 NO:89.

145. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
NO:90.

146. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
10 NO:91.

147. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
NO:92.  
15

148. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
NO:93.

149. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
20 NO:94.

150. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
NO:95.

151. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
25 NO:96.

152. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
NO:97.  
30

153. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
NO:98.

154. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
35 NO:99.

155. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
NO:100.

5 156. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
NO:101.

157. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
NO:102.

10 158. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
NO:103.

159. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
NO:104.

15 160. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
NO:105.

20 161. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
NO:106.

162. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
NO:107.

25 163. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
NO:108.

164. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
NO:109.

30 165. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
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35 166. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID  
NO:111.

167. A polynucleotide of claim 12, comprising the polynucleotide sequence of SEQ ID NO:112.

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CHANG, Hsin-Ru

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Glu His Trp Thr Ser Gln Gly Gln Val Arg Met Arg Leu Phe Gly  
80 85 90  
Gln Arg Cys Gln Lys Cys Ser Trp Ser Gln Tyr Glu Met Pro Glu  
95 100 105  
Phe Ser Ser Asp Ser Thr Met Arg Ile Leu Ser Asn Leu Val Gln  
110 115 120  
His Ile Leu Lys Lys Tyr Tyr Gly Asn Gly Thr Arg Lys Ser Pro  
125 130 135  
Glu Met Pro Val Ile Leu Glu Val Ser Leu Glu Gly Ser His Asp  
140 145 150  
Thr Ala Asn Cys Glu Ala Cys Thr Leu Gly Ile Cys Gly Gln Gly  
155 160 165  
Leu Lys Ser Tyr Met Thr Lys Pro Ser Lys Ser Leu Leu Pro His  
170 175 180  
Leu Lys Thr Gly Asn Ser Ser Pro Gly Ile Gly Ala Val Tyr Leu  
185 190 195  
Ala Asn Gln Ala Lys Asn Gln Ser Ala Glu Ala Lys Glu Ala Lys  
200 205 210  
Gly Ser Gly Tyr Glu Lys Leu Gly Pro Ser Arg Asp Pro Asp Pro  
215 220 225  
Leu Asn Ile Cys Val Phe Ile Leu Leu Leu Val Phe Ile Val Val  
230 235 240  
Lys Cys Phe Thr Ser Glu  
245

<210> 2  
<211> 325

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte ID No: 1294096CD1

&lt;400&gt; 2

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Met Ala Leu Ala Asp Ser Thr Arg Gly Leu Pro Asn Gly Gly Gly
 1      5      10      15
Gly Gly Gly Gly Ser Gly Ser Ser Ser Ser Ala Glu Pro Pro
 20      25      30
Leu Phe Pro Asp Ile Val Glu Leu Asn Val Gly Gly Gln Val Tyr
 35      40      45
Val Thr Arg Arg Cys Thr Val Val Ser Val Pro Asp Ser Leu Leu
 50      55      60
Trp Arg Met Phe Thr Gln Gln Gln Pro Gln Glu Leu Ala Arg Asp
 65      70      75
Ser Lys Gly Arg Phe Phe Leu Asp Arg Asp Gly Phe Leu Phe Arg
 80      85      90
Tyr Ile Leu Asp Tyr Leu Arg Asp Leu Gln Leu Val Leu Pro Asp
 95      100     105
Tyr Phe Pro Glu Arg Ser Arg Leu Gln Arg Glu Ala Glu Tyr Phe
 110     115     120
Glu Leu Pro Glu Leu Val Arg Arg Leu Gly Ala Pro Gln Gln Pro
 125     130     135
Gly Pro Gly Pro Pro Pro Ser Arg Arg Gly Val His Lys Glu Gly
 140     145     150
Ser Leu Gly Asp Glu Leu Leu Pro Leu Gly Tyr Ser Glu Pro Glu
 155     160     165
Gln Gln Glu Gly Ala Ser Ala Gly Ala Pro Ser Pro Thr Leu Glu
 170     175     180
Leu Ala Ser Arg Ser Pro Ser Gly Gly Ala Ala Gly Pro Leu Leu
 185     190     195
Thr Pro Ser Gln Ser Leu Asp Gly Ser Arg Arg Ser Gly Tyr Ile
 200     205     210
Thr Ile Gly Tyr Arg Gly Ser Tyr Thr Ile Gly Arg Asp Ala Gln
 215     220     225
Ala Asp Ala Lys Phe Arg Arg Val Ala Arg Ile Thr Val Cys Gly
 230     235     240
Lys Thr Ser Leu Ala Lys Glu Val Phe Gly Asp Thr Leu Asn Glu
 245     250     255
Ser Arg Asp Pro Asp Arg Pro Pro Glu Arg Tyr Thr Ser Arg Tyr
 260     265     270
Tyr Leu Lys Phe Asn Phe Leu Glu Gln Ala Phe Asp Lys Leu Ser
 275     280     285
Glu Ser Gly Phe His Met Val Ala Cys Ser Ser Thr Gly Thr Cys
 290     295     300
Ala Phe Ala Ser Ser Thr Asp Gln Ser Glu Asp Lys Ile Trp Thr
 305     310     315
Ser Tyr Thr Glu Tyr Val Phe Cys Arg Glu
 320     325

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&lt;210&gt; 3

&lt;211&gt; 376

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte ID No: 7238537CD1

&lt;400&gt; 3

Met	Ala	Arg	Gly	Pro	Gly	Pro	Leu	Gly	Arg	Pro	Arg	Pro	Asp	Thr	
1				5					10					15	
Val	Ala	Met	Pro	Lys	Arg	Gly	Lys	Arg	Leu	Lys	Phe	Arg	Ala	His	
				20					25					30	
Asp	Ala	Cys	Ser	Gly	Arg	Val	Thr	Val	Ala	Asp	Tyr	Ala	Asn	Ser	
				35					40					45	
Asp	Pro	Ala	Val	Val	Arg	Ser	Gly	Arg	Val	Lys	Lys	Ala	Val	Ala	
				50					55					60	
Asn	Ala	Val	Gln	Gln	Glu	Val	Lys	Ser	Leu	Cys	Gly	Leu	Glu	Ala	
				65					70					75	
Ser	Gln	Val	Pro	Ala	Glu	Glu	Ala	Leu	Ser	Gly	Ala	Gly	Glu	Pro	
				80					85					90	
Cys	Asp	Ile	Ile	Asp	Ser	Ser	Asp	Glu	Met	Asp	Ala	Gln	Glu	Glu	
				95					100					105	
Ser	Ile	His	Glu	Arg	Thr	Val	Ser	Arg	Lys	Lys	Lys	Ser	Lys	Arg	
				110					115					120	
His	Lys	Glu	Glu	Leu	Asp	Gly	Ala	Gly	Gly	Glu	Glu	Tyr	Pro	Met	
				125					130					135	
Asp	Ile	Trp	Leu	Leu	Leu	Ala	Ser	Tyr	Ile	Arg	Pro	Glu	Asp	Ile	
				140					145					150	
Val	Asn	Phe	Ser	Leu	Ile	Cys	Lys	Asn	Ala	Trp	Thr	Val	Thr	Cys	
				155					160					165	
Thr	Ala	Ala	Phe	Trp	Thr	Arg	Leu	Tyr	Arg	Arg	His	Tyr	Thr	Leu	
				170					175					180	
Asp	Ala	Ser	Leu	Pro	Leu	Arg	Leu	Arg	Pro	Glu	Ser	Met	Glu	Lys	
				185					190					195	
Leu	Arg	Cys	Leu	Arg	Ala	Cys	Val	Ile	Arg	Ser	Leu	Tyr	His	Met	
				200					205					210	
Tyr	Glu	Pro	Phe	Ala	Ala	Arg	Ile	Ser	Lys	Asn	Pro	Ala	Ile	Pro	
				215					220					225	
Glu	Ser	Thr	Pro	Ser	Thr	Leu	Lys	Asn	Ser	Lys	Cys	Leu	Leu	Phe	
				230					235					240	
Trp	Cys	Arg	Lys	Ile	Val	Gly	Asn	Arg	Gln	Glu	Pro	Met	Trp	Glu	
				245					250					255	
Phe	Asn	Phe	Lys	Phe	Lys	Lys	Gln	Ser	Pro	Arg	Leu	Lys	Ser	Lys	
				260					265					270	
Cys	Thr	Gly	Gly	Leu	Gln	Pro	Pro	Val	Gln	Tyr	Glu	Asp	Val	His	
				275					280					285	
Thr	Asn	Pro	Asp	Gln	Asp	Cys	Cys	Leu	Leu	Gln	Val	Thr	Thr	Leu	
				290					295					300	
Asn	Phe	Ile	Phe	Ile	Pro	Ile	Val	Met	Gly	Met	Ile	Phe	Thr	Leu	
				305					310					315	
Phe	Thr	Ile	Asn	Val	Ser	Thr	Asp	Met	Arg	His	His	Arg	Val	Arg	
				320					325					330	
Leu	Val	Phe	Gln	Asp	Ser	Pro	Val	His	Gly	Gly	Arg	Lys	Leu	Arg	
				335					340					345	
Ser	Glu	Gln	Gly	Val	Gln	Val	Ile	Leu	Asp	Pro	Val	His	Ser	Val	
				350					355					360	
Arg	Leu	Phe	Asp	Trp	Trp	His	Pro	Gln	Tyr	Pro	Phe	Ser	Leu	Arg	
				365					370					375	
Ala															

&lt;210&gt; 4

&lt;211&gt; 461

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte ID No: 7494391CD1

&lt;400&gt; 4

Met	Lys	Ile	Leu	Phe	Val	Glu	Pro	Ala	Ile	Phe	Leu	Ser	Ala	Phe
1				5					10					15
Ala	Met	Thr	Leu	Thr	Gly	Pro	Leu	Thr	Thr	Gln	Tyr	Val	Tyr	Arg
				20					25					30
Arg	Ile	Trp	Glu	Glu	Thr	Gly	Asn	Tyr	Thr	Phe	Ser	Ser	Asp	Ser
				35					40					45
Asn	Ile	Ser	Glu	Cys	Glu	Lys	Asn	Lys	Ser	Ser	Pro	Ile	Phe	Ala
				50					55					60
Phe	Gln	Glu	Glu	Val	Gln	Lys	Lys	Val	Ser	Arg	Phe	Asn	Leu	Gln
				65					70					75
Met	Asp	Ile	Ser	Gly	Leu	Ile	Pro	Gly	Leu	Val	Ser	Thr	Phe	Ile
				80					85					90
Leu	Leu	Ser	Ile	Ser	Asp	His	Tyr	Gly	Arg	Lys	Phe	Pro	Met	Ile
				95					100					105
Leu	Ser	Ser	Val	Gly	Ala	Leu	Ala	Thr	Ser	Val	Trp	Leu	Cys	Leu
				110					115					120
Leu	Cys	Tyr	Phe	Ala	Phe	Pro	Phe	Gln	Leu	Leu	Ile	Ala	Ser	Thr
				125					130					135
Phe	Ile	Gly	Ala	Phe	Cys	Gly	Asn	Tyr	Thr	Thr	Phe	Trp	Gly	Ala
				140					145					150
Cys	Phe	Ala	Tyr	Ile	Val	Asp	Gln	Cys	Lys	Glu	His	Lys	Gln	Lys
				155					160					165
Thr	Ile	Arg	Ile	Ala	Ile	Ile	Asp	Phe	Leu	Leu	Gly	Leu	Val	Thr
				170					175					180
Gly	Leu	Thr	Gly	Leu	Ser	Ser	Gly	Tyr	Phe	Ile	Arg	Glu	Leu	Gly
				185					190					195
Phe	Glu	Trp	Ser	Phe	Leu	Ile	Ile	Ala	Val	Ser	Leu	Ala	Val	Asn
				200					205					210
Leu	Ile	Tyr	Ile	Leu	Phe	Phe	Leu	Gly	Asp	Pro	Val	Lys	Glu	Cys
				215					220					225
Ser	Ser	Gln	Asn	Val	Thr	Met	Ser	Cys	Ser	Glu	Gly	Phe	Lys	Asn
				230					235					240
Leu	Phe	Tyr	Arg	Thr	Tyr	Met	Leu	Phe	Lys	Asn	Ala	Ser	Gly	Lys
				245					250					255
Arg	Arg	Phe	Leu	Leu	Cys	Leu	Leu	Leu	Phe	Thr	Val	Ile	Thr	Tyr
				260					265					270
Phe	Phe	Val	Val	Ile	Gly	Ile	Ala	Pro	Ile	Phe	Ile	Leu	Tyr	Glu
				275					280					285
Leu	Asp	Ser	Pro	Leu	Cys	Trp	Asn	Glu	Val	Phe	Ile	Gly	Tyr	Gly
				290					295					300
Ser	Ala	Leu	Gly	Ser	Ala	Ser	Phe	Leu	Thr	Ser	Phe	Leu	Gly	Ile
				305					310					315
Trp	Leu	Phe	Ser	Tyr	Cys	Met	Glu	Asp	Ile	His	Met	Ala	Phe	Ile
				320					325					330
Gly	Ile	Phe	Thr	Thr	Met	Thr	Gly	Met	Ala	Met	Thr	Ala	Phe	Ala
				335					340					345
Ser	Thr	Thr	Leu	Met	Met	Phe	Leu	Ala	Arg	Val	Pro	Phe	Leu	Phe
				350					355					360
Thr	Ile	Val	Pro	Phe	Ser	Val	Leu	Arg	Ser	Met	Leu	Ser	Lys	Val
				365					370					375
Val	Arg	Ser	Thr	Glu	Gln	Gly	Thr	Leu	Phe	Ala	Cys	Ile	Ala	Phe
				380					385					390
Leu	Glu	Thr	Leu	Gly	Gly	Val	Thr	Ala	Val	Ser	Thr	Phe	Asn	Gly
				395					400					405
Ile	Tyr	Ser	Ala	Thr	Val	Ala	Trp	Tyr	Pro	Gly	Phe	Thr	Phe	Leu
				410					415					420
Leu	Ser	Ala	Gly	Leu	Leu	Leu	Leu	Pro	Ala	Ile	Ser	Leu	Cys	Val
				425					430					435
Val	Lys	Cys	Thr	Ser	Trp	Asn	Glu	Gly	Ser	Tyr	Glu	Leu	Leu	Ile
				440					445					450
Gln	Glu	Glu	Ser	Ser	Glu	Asp	Ala	Ser	Asp	Arg				
				455					460					



<210> 5  
 <211> 168  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte ID No: 6451054CD1

<400> 5  
 Met Met Glu Glu Ile Asp Arg Phe Gln Val Pro Thr Ala His Ser  
 1 5 10 15  
 Glu Met Gln Pro Leu Asp Pro Ala Ala Ser Ile Ser Asp Gly  
 20 25 30  
 Asp Cys Asp Ala Arg Glu Glu Lys Gln Arg Glu Leu Ala Arg Lys  
 35 40 45  
 Gly Ser Leu Lys Asn Gly Ser Met Gly Ser Pro Val Asn Gln Gln  
 50 55 60  
 Pro Lys Lys Asn Asn Val Met Ala Arg Thr Arg Leu Val Val Pro  
 65 70 75  
 Asn Lys Gly Tyr Ser Ser Leu Asp Gln Ser Pro Asp Glu Lys Pro  
 80 85 90  
 Leu Val Ala Leu Asp Thr Asp Ser Asp Asp Phe Asp Met Ser  
 95 100 105  
 Arg Tyr Ser Ser Ser Gly Tyr Ser Ser Ala Glu Gln Ile Asn Gln  
 110 115 120  
 Asp Leu Asn Ile Gln Leu Leu Lys Asp Gly Tyr Arg Leu Asp Glu  
 125 130 135  
 Ile Pro Asp Asp Glu Asp Leu Asp Leu Ile Pro Pro Lys Ser Val  
 140 145 150  
 Asn Pro Thr Cys Met Cys Cys Gln Ala Thr Ser Ser Thr Ala Cys  
 155 160 165  
 His Ile Gln

<210> 6  
 <211> 832  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte ID No: 7494592CD1

<400> 6  
 Met Met Glu Glu Glu Glu Leu Glu Phe Val Glu Glu Leu Glu Ala  
 1 5 10 15  
 Val Leu Gln Leu Thr Pro Glu Val Gln Leu Ala Ile Glu Gln Val  
 20 25 30  
 Phe Pro Ser Gln Asp Pro Leu Asp Arg Ala Asp Phe Asn Ala Val  
 35 40 45  
 Glu Tyr Ile Asn Thr Leu Phe Pro Thr Glu Gln Ser Leu Ala Asn  
 50 55 60  
 Ile Asp Glu Val Val Asn Lys Ile Arg Leu Lys Ile Arg Arg Leu  
 65 70 75  
 Asp Asp Asn Ile Arg Thr Val Val Arg Gly Gln Thr Asn Val Gly  
 80 85 90  
 Gln Asp Gly Arg Gln Ala Leu Glu Glu Ala Gln Lys Ala Ile Gln  
 95 100 105  
 Gln Leu Phe Gly Lys Ile Lys Asp Ile Lys Asp Lys Ala Glu Lys  
 110 115 120  
 Ser Glu Gln Met Val Lys Glu Ile Thr Arg Asp Ile Lys Gln Leu  
 125 130 135

Asp	His	Ala	Lys	Arg	His	Leu	Thr	Thr	Ser	Ile	Thr	Thr	Leu	Asn
				140					145					150
His	Leu	His	Met	Leu	Ala	Gly	Gly	Val	Asp	Ser	Leu	Glu	Ala	Met
				155					160					165
Thr	Arg	Arg	Arg	Gln	Tyr	Gly	Glu	Val	Ala	Asn	Leu	Leu	Gln	Gly
				170					175					180
Val	Met	Asn	Val	Leu	Glu	His	Phe	His	Lys	Tyr	Met	Gly	Ile	Pro
				185					190					195
Gln	Ile	Arg	Gln	Leu	Ser	Glu	Arg	Val	Lys	Ala	Ala	Gln	Thr	Glu
				200					205					210
Leu	Gly	Gln	Gln	Ile	Leu	Ala	Asp	Phe	Glu	Glu	Ala	Phe	Pro	Ser
				215					220					225
Gln	Gly	Thr	Lys	Arg	Pro	Gly	Gly	Pro	Ser	Asn	Val	Leu	Arg	Asp
				230					235					240
Ala	Cys	Leu	Val	Ala	Asn	Ile	Leu	Asp	Pro	Arg	Ile	Lys	Gln	Glu
				245					250					255
Ile	Ile	Lys	Lys	Phe	Ile	Lys	Gln	His	Leu	Ser	Glu	Tyr	Leu	Val
				260					265					270
Leu	Phe	Gln	Glu	Asn	Gln	Asp	Val	Ala	Trp	Leu	Asp	Lys	Ile	Asp
				275					280					285
Arg	Arg	Tyr	Ala	Trp	Ile	Lys	Arg	Gln	Leu	Val	Asp	Tyr	Glu	Glu
				290					295					300
Lys	Tyr	Gly	Arg	Met	Phe	Pro	Arg	Glu	Trp	Cys	Met	Ala	Glu	Arg
				305					310					315
Ile	Ala	Val	Glu	Phe	Cys	His	Val	Thr	Arg	Ala	Glu	Leu	Ala	Lys
				320					325					330
Ile	Met	Arg	Thr	Arg	Ala	Lys	Glu	Ile	Glu	Val	Lys	Leu	Leu	Leu
				335					340					345
Phe	Ala	Ile	Gln	Arg	Thr	Thr	Asn	Phe	Glu	Gly	Phe	Leu	Ala	Lys
				350					355					360
Arg	Phe	Ser	Gly	Cys	Thr	Leu	Thr	Asp	Gly	Thr	Leu	Lys	Lys	Leu
				365					370					375
Glu	Ser	Pro	Pro	Pro	Ser	Thr	Asn	Pro	Phe	Leu	Glu	Asp	Glu	Pro
				380					385					390
Thr	Pro	Glu	Met	Glu	Glu	Leu	Ala	Thr	Glu	Lys	Gly	Asp	Leu	Asp
				395					400					405
Gln	Pro	Lys	Lys	Pro	Lys	Ala	Pro	Asp	Asn	Pro	Phe	His	Gly	Ile
				410					415					420
Val	Ser	Lys	Cys	Phe	Glu	Pro	His	Leu	Tyr	Val	Tyr	Ile	Glu	Ser
				425					430					435
Gln	Asp	Lys	Asn	Leu	Gly	Glu	Leu	Ile	Asp	Arg	Phe	Val	Ala	Asp
				440					445					450
Phe	Lys	Ala	Gln	Gly	Pro	Pro	Lys	Pro	Asn	Thr	Asp	Glu	Gly	Gly
				455					460					465
Ala	Val	Leu	Pro	Ser	Cys	Ala	Asp	Leu	Phe	Val	Tyr	Tyr	Lys	Lys
				470					475					480
Cys	Met	Val	Gln	Cys	Ser	Gln	Leu	Ser	Thr	Gly	Glu	Pro	Met	Ile
				485					490					495
Ala	Leu	Thr	Thr	Ile	Phe	Gln	Lys	Tyr	Leu	Arg	Glu	Tyr	Ala	Trp
				500					505					510
Lys	Ile	Leu	Ser	Gly	Asn	Leu	Pro	Lys	Thr	Thr	Thr	Ser	Ser	Gly
				515					520					525
Gly	Leu	Thr	Ile	Ser	Ser	Leu	Leu	Lys	Glu	Lys	Glu	Gly	Ser	Glu
				530					535					540
Val	Ala	Lys	Phe	Thr	Leu	Glu	Glu	Leu	Cys	Leu	Ile	Cys	Asn	Ile
				545					550					555
Leu	Ser	Thr	Ala	Glu	Tyr	Cys	Leu	Ala	Thr	Thr	Gln	Gln	Leu	Glu
				560					565					570
Glu	Lys	Leu	Lys	Glu	Lys	Val	Asp	Val	Ser	Leu	Ile	Glu	Arg	Ile
				575					580					585
Asn	Leu	Thr	Gly	Glu	Met	Asp	Thr	Phe	Ser	Thr	Val	Ile	Ser	Ser
				590					595					600
Ser	Ile	Gln	Leu	Leu	Val	Gln	Asp	Leu	Asp	Ala	Ala	Cys	Asp	Pro

Ala Leu Thr Ala	Met Ser Lys Met Gln	Trp Gln Asn Val Glu	His
Val Gly Asp Gln	Ser Pro Tyr Val Thr	Ser Val Ile Leu His	Ile
Lys Gln Asn Val	Pro Ile Ile Arg Asp	Asn Leu Ala Ser Thr	Arg
Lys Tyr Phe Thr	Gln Phe Cys Val Lys	Phe Ala Asn Ser Phe	Ile
Pro Lys Phe Ile	Thr His Leu Phe Lys	Cys Lys Pro Ile Ser	Met
Val Gly Ala Glu	Gln Leu Leu Leu Asp	Thr His Ser Leu Lys	Met
Val Leu Leu Asp	Leu Pro Ser Ile Ser	Ser Gln Val Val Arg	Lys
Ala Pro Ala Ser	Tyr Thr Lys Ile Val	Val Lys Gly Met Thr	Arg
Ala Glu Met Ile	Leu Lys Val Val Met	Ala Pro His Glu Pro	Leu
Val Val Phe Val	Asp Asn Tyr Ile Lys	Leu Leu Thr Asp Cys	Asn
Thr Glu Thr Phe	Gln Lys Ile Leu Asp	Met Lys Gly Leu Lys	Arg
Ser Glu Gln Ser	Ser Met Leu Glu Leu	Leu Arg Gln Arg Leu	Pro
Ala Pro Pro Ser	Gly Ala Glu Ser Ser	Gly Ser Leu Ser Leu	Thr
Ala Pro Thr Pro	Glu Gln Glu Ser Ser	Arg Ile Arg Lys Leu	Glu
Lys Leu Ile Lys	Lys Arg Leu		

&lt;210&gt; 7

&lt;211&gt; 393

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte ID No: 5202657CD1

&lt;400&gt; 7

Met Glu Gln Cys	Ala Cys Val Glu Arg	Glu Leu Asp Lys Val	Leu
Gln Lys Phe Leu	Thr Tyr Gly Gln His	Cys Glu Arg Ser Leu	Glu
Glu Leu Leu His	Tyr Val Gly Gln Leu	Arg Ala Glu Leu Ala	Ser
Ala Ala Leu Gln	Gly Thr Pro Leu Ser	Ala Thr Leu Ser Leu	Val
Met Ser Gln Cys	Cys Arg Lys Ile Lys	Asp Thr Val Gln Lys	Leu
Ala Ser Asp His	Lys Asp Ile His Ser	Ser Val Ser Arg Val	Gly
Lys Ala Ile Asp	Arg Asn Phe Asp Ser	Glu Ile Cys Gly Val	Val
Ser Asp Ala Val	Trp Asp Ala Arg Glu	Gln Gln Gln Ile Leu	Ser
Gln Met Ala Ile	Val Glu His Leu Tyr	Gln Gln Gly Met Leu	Ser
Val Ala Glu Glu	Leu Cys Gln Glu Ser	Thr Leu Asn Val Asp	Leu
Asp Phe Lys Gln	Pro Phe Leu Glu Leu	Asn Arg Ile Leu Glu	Ala

155	160	165
Leu His Glu Gln Asp Leu Gly Pro Ala	Leu Glu Trp Ala Val Ser	
170	175	180
His Arg Gln Arg Leu Leu Glu Leu Asn	Ser Ser Leu Glu Phe Lys	
185	190	195
Leu His Arg Leu His Phe Ile Arg Leu	Leu Ala Gly Gly Pro Ala	
200	205	210
Lys Gln Leu Glu Ala Leu Ser Tyr Ala	Arg His Phe Gln Pro Phe	
215	220	225
Ala Arg Leu His Gln Arg Glu Ile Gln	Val Met Met Gly Ser Leu	
230	235	240
Val Tyr Leu Arg Leu Gly Leu Glu Lys	Ser Pro Tyr Cys His Leu	
245	250	255
Leu Asp Ser Ser His Trp Ala Glu Ile	Cys Glu Thr Phe Thr Arg	
260	265	270
Asp Ala Cys Ser Leu Leu Gly Leu Ser	Val Glu Ser Pro Leu Ser	
275	280	285
Val Ser Phe Ala Ser Gly Cys Val Ala	Leu Pro Val Leu Met Asn	
290	295	300
Ile Lys Ala Val Ile Glu Gln Arg Gln	Cys Thr Gly Val Trp Asn	
305	310	315
His Lys Asp Glu Leu Pro Ile Glu Ile	Glu Leu Gly Met Lys Cys	
320	325	330
Trp Tyr His Ser Val Phe Ala Cys Pro	Ile Leu Arg Gln Gln Thr	
335	340	345
Ser Asp Ser Asn Pro Pro Ile Lys Leu	Ile Cys Gly His Val Ile	
350	355	360
Ser Arg Asp Ala Leu Asn Lys Leu Ile	Asn Gly Gly Lys Leu Lys	
365	370	375
Cys Pro Tyr Cys Pro Met Glu Gln Asn	Pro Ala Asp Gly Lys Arg	
380	385	390
Ile Ile Phe		

&lt;210&gt; 8

&lt;211&gt; 280

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte ID No: 2013529CD1

&lt;400&gt; 8

Met Ala Thr Glu Ala Pro Val Asn Ile Ala Pro Pro Glu Cys Ser	
1 5 10 15	
Thr Val Val Ser Thr Ala Val Asp Ser Leu Ile Trp Gln Pro Asn	
20 25 30	
Ser Leu Asn Met His Met Ile Arg Pro Lys Ser Ala Lys Gly Arg	
35 40 45	
Thr Arg Pro Ser Leu Gln Lys Ser Gln Gly Val Glu Val Cys Ala	
50 55 60	
His His Ile Pro Ser Pro Pro Pro Ala Ile Pro Tyr Glu Leu Pro	
65 70 75	
Ser Ser Gln Lys Pro Gly Ala Cys Ala Pro Lys Ser Pro Asn Gln	
80 85 90	
Gly Ala Ser Asp Glu Ile Pro Glu Leu Gln Gln Gln Val Pro Thr	
95 100 105	
Gly Ala Ser Ser Ser Leu Asn Lys Tyr Pro Val Leu Pro Ser Ile	
110 115 120	
Asn Arg Lys Asn Leu Glu Glu Glu Ala Val Glu Thr Val Ala Lys	
125 130 135	
Lys Ala Ser Ser Leu Gln Leu Ser Ser Ile Arg Ala Leu Tyr Gln	

	140		145		150
Asp Glu Thr Gly Thr Met Lys Thr Ser	Glu Glu Asp Ser Arg Ala				
	155		160		165
Arg Ala Cys Ala Val Glu Arg Lys Phe	Ile Val Arg Thr Lys Lys				
	170		175		180
Gln Gly Ser Ser Arg Ala Gly Asn Leu	Glu Glu Pro Ser Asp Gln				
	185		190		195
Glu Pro Arg Leu Leu Leu Ala Val Arg	Ser Pro Thr Gly Gln Arg				
	200		205		210
Phe Val Arg His Phe Arg Pro Thr Asp	Asp Leu Gln Thr Ile Val				
	215		220		225
Ala Val Ala Glu Gln Lys Asn Lys Thr	Ser Tyr Arg His Cys Ser				
	230		235		240
Ile Glu Thr Met Glu Val Pro Arg Arg	Arg Phe Ser Asp Leu Thr				
	245		250		255
Lys Ser Leu Gln Glu Cys Arg Ile Pro	His Lys Ser Val Leu Gly				
	260		265		270
Ile Ser Leu Glu Asp Gly Glu Gly Trp	Pro				
	275		280		

&lt;210&gt; 9

&lt;211&gt; 344

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte ID No: 3841351CD1

&lt;400&gt; 9

Met Asp Ser Tyr Ser Ala Pro Glu Ser Thr	Pro Ser Ala Ser Ser
1	5 10 15
Arg Pro Glu Asp Tyr Phe Ile Gly Ala Thr	Pro Leu Gln Lys Arg
	20 25 30
Leu Glu Ser Val Arg Lys Gln Ser Ser Phe	Ile Leu Thr Pro Pro
	35 40 45
Arg Arg Lys Ile Pro Gln Cys Ser Gln Leu	Gln Glu Asp Val Asp
	50 55 60
Pro Gln Lys Val Ala Phe Leu Leu His Lys	Gln Trp Thr Leu Tyr
	65 70 75
Ser Leu Thr Pro Leu Tyr Lys Phe Ser Tyr	Ser Asn Leu Lys Glu
	80 85 90
Tyr Ser Arg Leu Leu Asn Ala Phe Ile Val	Ala Glu Lys Gln Lys
	95 100 105
Gly Leu Ala Val Glu Val Gly Glu Asp Phe	Asn Ile Lys Val Ile
	110 115 120
Phe Ser Thr Leu Leu Gly Met Lys Gly Thr	Gln Arg Asp Pro Glu
	125 130 135
Ala Phe Leu Val Gln Ile Val Ser Lys Ser	Gln Leu Pro Ser Glu
	140 145 150
Asn Arg Glu Gly Lys Val Leu Trp Thr Gly	Trp Phe Cys Cys Val
	155 160 165
Phe Gly Asp Ser Leu Leu Glu Thr Val Ser	Glu Asp Phe Thr Cys
	170 175 180
Leu Pro Leu Phe Leu Ala Asn Gly Ala Glu	Ser Asn Thr Ala Ile
	185 190 195
Ile Gly Thr Trp Phe Gln Lys Thr Phe Asp	Cys Tyr Phe Ser Pro
	200 205 210
Leu Ala Ile Asn Ala Phe Asn Leu Ser Trp	Met Ala Ala Met Trp
	215 220 225
Thr Ala Cys Lys Met Asp His Tyr Val Ala	Thr Thr Glu Phe Leu
	230 235 240
Trp Ser Val Pro Cys Ser Pro Gln Ser Leu	Asp Ile Ser Phe Ala

Ile His Pro Glu Asp	245	Ala Lys Ala Leu	250	Trp Asp Ser Val His	255
Thr Pro Gly Glu Val	260	Thr Gln Glu Glu	265	Val Asp Leu Phe Met	270
Cys Leu Tyr Ser His	275	Phe His Arg His	280	Phe Lys Ile His Leu	285
Ala Thr Arg Leu Val	290	Arg Val Ser Thr	295	Ser Val Ala Ser Ala	300
Thr Asp Gly Lys Ile	305	Lys Ile Leu Cys	310	His Lys Tyr Leu Ile	315
Val Leu Ala Tyr Leu	320	Thr Glu Leu Ala	325	Ile Phe Gln Ile Glu	330
	335		340		

&lt;210&gt; 10

&lt;211&gt; 405

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte ID No: 152116CD1

&lt;400&gt; 10

Met Glu Pro Gly Ala	5	Gly Gly Arg Asn Thr	10	Ala Arg Ala Gln Arg	15
Ala Gly Ser Pro Asn	20	Thr Pro Pro Pro Arg	25	Glu Gln Glu Arg Lys	30
Leu Glu Gln Glu Lys	35	Leu Ser Gly Val Val	40	Lys Ser Val His Arg	45
Arg Leu Arg Lys Lys	50	Tyr Arg Glu Val Gly	55	Asp Phe Asp Lys Ile	60
Trp Arg Glu His Cys	65	Glu Asp Glu Glu Thr	70	Leu Cys Glu Tyr Ala	75
Val Ala Met Lys Asn	80	Leu Ala Asp Asn His	85	Trp Ala Lys Thr Cys	90
Glu Gly Glu Gly Arg	95	Ile Glu Trp Cys Cys	100	Ser Val Cys Arg Glu	105
Tyr Phe Gln Asn Gly	110	Gly Lys Arg Lys Ala	115	Leu Glu Lys Asp Glu	120
Lys Arg Ala Val Leu	125	Ala Thr Lys Thr Thr	130	Pro Ala Leu Asn Met	135
His Glu Ser Ser Gln	140	Leu Glu Gly His Leu	145	Thr Asn Leu Ser Phe	150
Thr Asn Pro Glu Phe	155	Ile Thr Glu Leu Leu	160	Gln Ala Ser Gly Lys	165
Ile Arg Leu Leu Asp	170	Val Gly Ser Cys Phe	175	Asn Pro Phe Leu Lys	180
Phe Glu Glu Phe Leu	185	Thr Val Gly Ile Asp	190	Ile Val Pro Ala Val	195
Glu Ser Val Tyr Lys	200	Cys Asp Phe Leu Asn	205	Leu Gln Leu Gln Gln	210
Pro Leu Gln Leu Ala	215	Gln Asp Ala Ile Asp	220	Ala Phe Leu Lys Gln	225
Leu Lys Asn Pro Ile	230	Asp Ser Leu Pro Gly	235	Glu Leu Phe His Val	240
Val Val Phe Ser Leu	245	Leu Leu Ser Tyr Phe	250	Pro Ser Pro Tyr Gln	255
Arg Trp Ile Cys Cys	260	Lys Lys Ala His Glu	265	Leu Leu Val Leu Asn	270
Gly Leu Leu Leu Ile	275	Ile Thr Pro Asp Ser	280	Ser Ser His Gln Asn	285
His Ala Met Met Met		Lys Ser Trp Lys Ile		Ala Ile Glu Ser Leu	

	290		295		300
Gly Phe Lys Arg Phe	Lys Tyr Ser Lys	Phe Ser His Met His	Leu		
	305		310		315
Met Ala Phe Arg Lys	Ile Ser Leu Lys	Thr Thr Ser Asp Leu	Val		
	320		325		330
Ser Arg Asn Tyr Pro	Gly Met Leu Tyr	Ile Pro Gln Asp Phe	Asn		
	335		340		345
Ser Ile Glu Asp Glu	Glu Tyr Ser Asn	Pro Ser Cys Tyr Val	Arg		
	350		355		360
Ser Asp Ile Glu Asp	Glu Gln Leu Ala	Tyr Gly Phe Thr Glu	Leu		
	365		370		375
Pro Asp Ala Pro Tyr	Asp Ser Asp Ser	Gly Glu Ser Gln Ala	Ser		
	380		385		390
Ser Ile Pro Phe Tyr	Glu Leu Glu Asp	Pro Ile Leu Leu Leu	Ser		
	395		400		405

<210> 11  
 <211> 185  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte ID No: 2381031CD1

<400> 11	
Met Glu Val His Gly	Lys Pro Lys Ala Ser Pro Ser Cys Ser Ser
1	5 10 15
Pro Thr Arg Asp Ser	Ser Gly Val Pro Val Ser Lys Glu Leu Leu
	20 25 30
Thr Ala Gly Ser Asp	Gly Arg Gly Gly Ile Trp Asp Arg Leu Leu
	35 40 45
Ile Asn Ser Gln Pro	Lys Ser Arg Lys Thr Ser Thr Leu Gln Thr
	50 55 60
Val Arg Ile Glu Arg	Ser Pro Leu Leu Asp Gln Val Gln Thr Phe
	65 70 75
Leu Pro Gln Met Ala	Arg Ala Asn Glu Lys Leu Arg Lys Glu Met
	80 85 90
Ala Ala Ala Pro Gly	Arg Phe Asn Ile Glu Asn Ile Asp Gly
	95 100 105
Pro His Ser Lys Val	Ile Gln Met Asp Val Ala Leu Phe Glu Met
	110 115 120
Asn Gln Ser Asp Ser	Lys Glu Val Asp Ser Ser Glu Glu Ser Ser
	125 130 135
Gln Asp Ser Ser Glu	Asn Ser Ser Glu Ser Glu Asp Glu Asp Asp
	140 145 150
Ser Ile Pro Ser Glu	Val Thr Ile Asp Asn Ile Lys Leu Pro Asn
	155 160 165
Ser Glu Gly Gly Lys	Gly Lys Ile Glu Val Leu Asp Ser Pro Ala
	170 175 180
Ser Lys Lys Lys Lys	
	185

<210> 12  
 <211> 463  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte ID No: 2511371CD1

&lt;400&gt; 12

Met	Ala	Gln	Gln	Gln	Thr	Gly	Ser	Arg	Lys	Arg	Lys	Ala	Pro	Ala	
1				5					10					15	
Val	Glu	Ala	Asp	Ala	Glu	Ser	Ser	Pro	Ser	Gln	Gly	Leu	Ala	Ala	
			20						25					30	
Ala	Asp	Gly	Glu	Gly	Pro	Leu	Leu	Leu	Lys	Arg	Gln	Arg	Arg	Pro	
			35						40					45	
Ala	Thr	Tyr	Arg	Ser	Met	Ala	His	Tyr	Leu	Lys	Val	Arg	Glu	Val	
			50						55					60	
Gly	Gly	Trp	Gly	Pro	Ala	Arg	Leu	Gln	Gly	Phe	Asp	Gly	Glu	Leu	
			65						70					75	
Arg	Gly	Tyr	Ala	Val	Gln	Arg	Leu	Pro	Glu	Leu	Leu	Thr	Glu	Arg	
			80						85					90	
Gln	Leu	Glu	Leu	Gly	Thr	Val	Asn	Lys	Val	Phe	Ala	Ser	Gln	Trp	
			95						100					105	
Leu	Asn	Ser	Arg	Gln	Val	Val	Cys	Gly	Thr	Lys	Cys	Asn	Thr	Leu	
			110						115					120	
Phe	Val	Val	Asp	Val	Glu	Ser	Gly	His	Ile	Ala	Arg	Ile	Pro	Leu	
			125						130					135	
Leu	Arg	Asp	Ser	Glu	Ala	Arg	Leu	Ala	Gln	Asp	Gln	Gln	Gly	Cys	
			140						145					150	
Gly	Ile	His	Ala	Ile	Glu	Leu	Asn	Pro	Ser	Lys	Thr	Leu	Leu	Ala	
			155						160					165	
Thr	Gly	Gly	Glu	Asn	Pro	Asn	Ser	Leu	Ala	Ile	Tyr	Gln	Leu	Pro	
			170						175					180	
Ser	Leu	Asp	Pro	Leu	Cys	Leu	Gly	Asp	Arg	His	Gly	His	Lys	Asp	
			185						190					195	
Trp	Ile	Phe	Ala	Val	Ala	Trp	Leu	Ser	Asp	Thr	Val	Ala	Val	Ser	
			200						205					210	
Gly	Ser	Arg	Asp	Gly	Thr	Val	Ala	Leu	Trp	Arg	Met	Asp	Pro	Asp	
			215						220					225	
Lys	Phe	Asp	Asp	Thr	Val	Ala	Trp	His	Ser	Glu	Val	Gly	Leu	Pro	
			230						235					240	
Val	Tyr	Ala	His	Ile	Arg	Pro	Arg	Asp	Val	Glu	Ala	Ile	Pro	Arg	
			245						250					255	
Ala	Ile	Ile	Asn	Pro	Ser	Asn	Arg	Lys	Val	Arg	Ala	Leu	Ala	Cys	
			260						265					270	
Gly	Gly	Lys	Asn	Gln	Glu	Leu	Gly	Ala	Val	Ser	Leu	Asp	Gly	Tyr	
			275						280					285	
Phe	His	Leu	Trp	Lys	Ala	Gly	Ser	Ala	Leu	Ser	Arg	Leu	Leu	Ser	
			290						295					300	
Ile	Arg	Leu	Pro	Tyr	Phe	Arg	Asp	Asn	Val	Cys	Leu	Thr	Tyr	Cys	
			305						310					315	
Asp	Asp	Met	Ser	Val	Tyr	Ala	Val	Gly	Ser	His	Ser	His	Val	Ser	
			320						325					330	
Phe	Leu	Asp	Leu	Arg	Gln	Asp	Gln	Gln	Asn	Ile	Arg	Pro	Leu	Cys	
			335						340					345	
Ser	Arg	Glu	Gly	Gly	Thr	Gly	Val	Arg	Ser	Leu	Ser	Phe	Tyr	Arg	
			350						355					360	
His	Ile	Ile	Thr	Val	Gly	Thr	Gly	Gln	Gly	Ser	Leu	Leu	Phe	Tyr	
			365						370					375	
Asp	Val	Arg	Ala	Gln	Lys	Phe	Leu	Glu	Glu	Arg	Ala	Ser	Ala	Thr	
			380						385					390	
Leu	Glu	Ser	Ser	Ser	Gly	Pro	Ala	Arg	Arg	Lys	Leu	Arg	Leu	Ala	
			395						400					405	
Cys	Gly	Arg	Gly	Trp	Leu	Asn	His	Asn	Asp	Phe	Trp	Val	Asn	Tyr	
			410						415					420	
Phe	Gly	Gly	Met	Glu	Val	Phe	Pro	Asn	Ala	Leu	Tyr	Thr	His	Cys	
			425						430					435	
Tyr	Asn	Trp	Pro	Glu	Met	Lys	Leu	Phe	Val	Ala	Gly	Gly	Pro	Leu	
			440						445					450	
Pro	Ala	Gly	Leu	His	Gly	Asn	Tyr	Ala	Gly	Leu	Trp	Ser			
			455						460						



<210> 13  
 <211> 403  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte ID No: 8068623CD1

<400> 13

Met	Ala	Leu	Arg	Ser	Ala	Gln	Gly	Asp	Gly	Pro	Thr	Ser	Gly	His
1				5					10					15
Trp	Asp	Gly	Gly	Ala	Glu	Lys	Ala	Asp	Phe	Asn	Ala	Lys	Arg	Lys
				20					25					30
Lys	Lys	Val	Ala	Glu	Ile	His	Gln	Ala	Leu	Asn	Ser	Asp	Pro	Thr
				35					40					45
Asp	Val	Ala	Ala	Leu	Arg	Arg	Met	Ala	Ile	Ser	Glu	Gly	Gly	Leu
				50					55					60
Leu	Thr	Asp	Glu	Ile	Arg	Arg	Lys	Val	Trp	Pro	Lys	Leu	Leu	Asn
				65					70					75
Val	Asn	Ala	Asn	Asp	Pro	Pro	Pro	Ile	Ser	Gly	Lys	Asn	Leu	Arg
				80					85					90
Gln	Met	Ser	Lys	Asp	Tyr	Gln	Gln	Val	Leu	Leu	Asp	Val	Arg	Arg
				95					100					105
Ser	Leu	Arg	Arg	Phe	Pro	Pro	Gly	Met	Pro	Glu	Glu	Gln	Arg	Glu
				110					115					120
Gly	Leu	Gln	Glu	Glu	Leu	Ile	Asp	Ile	Ile	Leu	Leu	Ile	Leu	Glu
				125					130					135
Arg	Asn	Pro	Gln	Leu	His	Tyr	Tyr	Gln	Gly	Tyr	His	Asp	Ile	Val
				140					145					150
Val	Thr	Phe	Leu	Leu	Val	Val	Gly	Glu	Arg	Leu	Ala	Thr	Ser	Leu
				155					160					165
Val	Glu	Lys	Leu	Ser	Thr	His	His	Leu	Arg	Asp	Phe	Met	Asp	Pro
				170					175					180
Thr	Met	Asp	Asn	Thr	Lys	His	Ile	Leu	Asn	Tyr	Leu	Met	Pro	Ile
				185					190					195
Ile	Asp	Gln	Val	Asn	Pro	Glu	Leu	His	Asp	Phe	Met	Gln	Ser	Ala
				200					205					210
Glu	Val	Gly	Thr	Ile	Phe	Ala	Leu	Ser	Trp	Leu	Ile	Thr	Trp	Phe
				215					220					225
Gly	His	Val	Leu	Ser	Asp	Phe	Arg	His	Val	Val	Arg	Leu	Tyr	Asp
				230					235					240
Phe	Phe	Leu	Ala	Cys	His	Pro	Leu	Met	Pro	Ile	Tyr	Phe	Ala	Ala
				245					250					255
Val	Ile	Val	Leu	Tyr	Arg	Glu	Gln	Glu	Val	Leu	Asp	Cys	Asp	Cys
				260					265					270
Asp	Met	Ala	Ser	Val	His	His	Leu	Leu	Ser	Gln	Ile	Pro	Gln	Asp
				275					280					285
Leu	Pro	Tyr	Glu	Thr	Leu	Ile	Ser	Arg	Ala	Gly	Asp	Leu	Phe	Val
				290					295					300
Gln	Phe	Pro	Pro	Ser	Glu	Leu	Ala	Arg	Glu	Ala	Ala	Ala	Gln	Gln
				305					310					315
Gln	Ala	Glu	Arg	Thr	Ala	Ala	Ser	Thr	Phe	Lys	Asp	Phe	Glu	Leu
				320					325					330
Ala	Ser	Ala	Gln	Gln	Arg	Pro	Asp	Met	Val	Leu	Arg	Gln	Arg	Phe
				335					340					345
Arg	Gly	Leu	Leu	Arg	Pro	Glu	Asp	Arg	Thr	Lys	Asp	Val	Leu	Thr
				350					355					360
Lys	Pro	Arg	Thr	Asn	Arg	Phe	Val	Lys	Leu	Ala	Val	Met	Gly	Leu
				365					370					375
Thr	Val	Ala	Leu	Gly	Ala	Ala	Ala	Leu	Ala	Val	Val	Lys	Ser	Ala
				380					385					390
Leu	Glu	Trp	Ala	Pro	Lys	Phe	Gln	Leu	Gln	Leu	Phe	Pro		

395

400

&lt;210&gt; 14

&lt;211&gt; 574

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte ID No: 677977CD1

&lt;400&gt; 14

Met	Gly	Gly	Glu	Arg	Lys	Ala	Gln	Thr	Cys	Ala	Ala	Thr	Phe	Ser
1				5					10					15
Val	Pro	Ala	Arg	Ala	Cys	Ala	Ala	Gly	Ser	Arg	Thr	Met	Pro	Thr
			20						25					30
Cys	Ala	Gly	Ser	Trp	Ser	Ser	Trp	Ala	Val	Arg	Trp	Ala	Leu	Ser
			35						40					45
Ala	Arg	Arg	Cys	Gly	Trp	Pro	Thr	Arg	Arg	Arg	Ser	Thr	Ala	Pro
			50						55					60
Cys	Thr	Pro	Gly	Ser	Trp	Arg	Cys	Ala	Thr	Thr	Gly	Cys	Arg	Cys
			65						70					75
Leu	Ala	Arg	Ser	Ser	Arg	Arg	Ser	Arg	Gly	Leu	Arg	Ala	Pro	Asp
			80						85					90
Leu	Arg	Ala	Arg	Val	His	Leu	Gln	Gly	Gln	Pro	Arg	Leu	Val	Leu
			95						100					105
Ala	Leu	Ala	Glu	Ala	Pro	Arg	His	Leu	Gln	Pro	Ala	Leu	Leu	Arg
			110						115					120
Arg	Gly	Gly	Pro	Pro	Ala	Pro	Ser	Pro	Ala	Pro	Gly	Pro	Pro	Val
			125						130					135
Lys	Glu	Glu	Pro	Ala	Leu	Pro	Ser	Gly	Ala	Gly	Pro	Leu	Pro	Asp
			140						145					150
Arg	Ala	Pro	Ala	Pro	Pro	Pro	Pro	Ala	Glu	Gly	Gly	Tyr	Gly	Asp
			155						160					165
Glu	Gln	Ile	Tyr	Ser	Ala	Ser	Val	Thr	Gly	Leu	Tyr	Trp	Lys	Leu
			170						175					180
Leu	Pro	Glu	Gln	Ala	Ala	Pro	Pro	Gly	Ala	Gly	Asp	Pro	Gly	Ala
			185						190					195
Gly	Gly	Cys	Gly	Arg	Arg	Trp	Arg	Gly	Asp	Arg	Val	Thr	Val	Leu
			200						205					210
Leu	Ala	Ala	Asn	Leu	Thr	Gly	Ser	His	Lys	Leu	Lys	Pro	Leu	Val
			215						220					225
Ile	Gly	Arg	Leu	Pro	Asp	Pro	Pro	Ser	Leu	Arg	His	His	Asn	Gln
			230						235					240
Asp	Lys	Phe	Pro	Ala	Ser	Tyr	Arg	Tyr	Ser	Pro	Asp	Ala	Trp	Leu
			245						250					255
Ser	Arg	Pro	Leu	Leu	Arg	Gly	Trp	Phe	Phe	Glu	Glu	Phe	Val	Pro
			260						265					270
Gly	Val	Lys	Arg	Tyr	Leu	Arg	Arg	Ser	Cys	Leu	Gln	Gln	Lys	Ala
			275						280					285
Val	Leu	Leu	Val	Ala	His	Pro	Pro	Cys	Pro	Ser	Pro	Ala	Ala	Ser
			290						295					300
Met	Pro	Ala	Leu	Asp	Ser	Glu	Asp	Ala	Pro	Val	Arg	Cys	Arg	Pro
			305						310					315
Glu	Pro	Leu	Gly	Pro	Pro	Glu	Glu	Leu	Gln	Thr	Pro	Asp	Gly	Ala
			320						325					330
Val	Arg	Val	Leu	Phe	Leu	Ser	Lys	Gly	Ser	Ser	Arg	Ala	His	Ile
			335						340					345
Pro	Glu	Pro	Val	Glu	Gln	Gly	Val	Val	Ala	Ala	Phe	Lys	Gln	Leu
			350						355					360
Tyr	Lys	Arg	Glu	Leu	Leu	Arg	Leu	Ala	Val	Ser	Cys	Ala	Ser	Gly
			365						370					375
Ser	Pro	Leu	Asp	Phe	Met	Arg	Ser	Phe	Met	Leu	Lys	Asp	Met	Leu

	380		385		390
Tyr Leu Ala Gly	Leu Ser Trp Asp Leu	Val Gln Ala Gly Ser	Ile		
	395		400		405
Glu Arg Cys Trp	Leu Leu Gly Leu Arg	Ala Ala Phe Glu Pro	Arg		
	410		415		420
Pro Gly Glu Asp	Ser Ala Gly Gln Pro	Ala Gln Ala Glu Glu	Ala		
	425		430		435
Ala Glu His Ser	Arg Val Leu Ser Asp	Leu Thr His Leu Ala	Ala		
	440		445		450
Leu Ala Tyr Lys	Cys Leu Ala Pro Glu	Glu Val Ala Glu Trp	Leu		
	455		460		465
His Leu Asp Asp	Asp Gly Ala Ser Leu	Pro Ser Ala Met Gly	Gly		
	470		475		480
Gly Glu Asp Glu	Glu Glu Ala Thr Asp	Tyr Gly Gly Thr Ser	Ser		
	485		490		495
Leu Pro Ser Ala	Ile Gly Gly Gly Glu	Asp Glu Glu Glu Ala	Thr		
	500		505		510
Asp Tyr Gly Gly	Thr Ser Val Pro Thr	Ala Gly Glu Ala Val	Arg		
	515		520		525
Gly Leu Glu Thr	Ala Leu Arg Trp Leu	Glu Asn Gln Asp Pro	Arg		
	530		535		540
Glu Val Gly Pro	Leu Arg Leu Val Gln	Leu Arg Ser Leu Ile	Ser		
	545		550		555
Met Ala Arg Arg	Leu Gly Gly Ile Gly	His Thr Pro Ala Gly	Pro		
	560		565		570
Tyr Asp Gly Val					

&lt;210&gt; 15

&lt;211&gt; 731

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte ID No: 1661472CD1

&lt;400&gt; 15

Met Gln Gly Asp Pro	Asp Asp Thr Ser	His Arg Gly His Pro	Leu	
1	5	10	15	
Cys Lys Phe Cys Asp	Glu Arg Tyr Leu	Asn Asp Glu Leu	Leu	
	20	25	30	
Lys His Leu Arg Arg	Asp His Tyr Phe	Cys His Phe Cys Asp	Ser	
	35	40	45	
Asp Gly Ala Gln Asp	Tyr Tyr Ser Asp	Tyr Ala Tyr Leu Arg	Glu	
	50	55	60	
His Phe Arg Glu Lys	His Phe Leu Cys	Glu Glu Gly Arg Cys	Ser	
	65	70	75	
Thr Glu Gln Phe Thr	His Ala Phe Arg	Thr Glu Ile Asp Leu	Lys	
	80	85	90	
Ala His Arg Thr Ala	Cys His Ser Arg	Ser Arg Ala Glu Ala	Arg	
	95	100	105	
Gln Asn Arg His Ile	Asp Leu Gln Phe	Ser Tyr Ala Pro Arg	His	
	110	115	120	
Ser Arg Arg Asn Glu	Gly Val Val Gly	Gly Glu Asp Tyr Glu	Glu	
	125	130	135	
Val Asp Arg Tyr Ser	Arg Gln Gly Arg	Val Ala Arg Ala Gly	Thr	
	140	145	150	
Arg Gly Ala Gln Gln	Ser Arg Arg Gly	Ser Trp Arg Tyr Lys	Arg	
	155	160	165	
Glu Glu Glu Asp Arg	Glu Val Ala Ala	Ala Val Arg Ala Ser	Val	
	170	175	180	
Ala Ala Gln Gln Gln	Glu Glu Ala Arg	Arg Ser Glu Asp Gln	Glu	

	185		190		195
Glu Gly Gly Arg	Pro Lys Lys Glu Glu	Ala Ala Ala Arg Gly	Pro		
	200		205		210
Glu Asp Pro Arg	Gly Pro Arg Arg Ser	Pro Arg Thr Gln Gly	Glu		
	215		220		225
Gly Pro Gly Pro	Lys Glu Thr Ser Thr	Asn Gly Pro Val Ser	Gln		
	230		235		240
Glu Ala Phe Ser	Val Thr Gly Pro Ala	Ala Pro Gly Cys Val	Gly		
	245		250		255
Val Pro Gly Ala	Leu Pro Pro Pro Ser	Pro Lys Leu Lys Asp	Glu		
	260		265		270
Asp Phe Pro Ser	Leu Ser Ala Ser Thr	Ser Ser Ser Cys Ser	Thr		
	275		280		285
Ala Ala Thr Pro	Gly Pro Val Gly Leu	Ala Leu Pro Tyr Ala	Ile		
	290		295		300
Pro Ala Arg Gly	Arg Ser Ala Phe Gln	Glu Glu Asp Phe Pro	Ala		
	305		310		315
Leu Val Ser Ser	Val Pro Lys Pro Gly	Thr Ala Pro Thr Ser	Leu		
	320		325		330
Val Ser Ala Trp	Asn Ser Ser Ser Ser	Ser Lys Lys Val Ala	Gln		
	335		340		345
Pro Pro Leu Ser	Ala Gln Ala Thr Gly	Ser Gly Gln Pro Thr	Arg		
	350		355		360
Lys Ala Gly Lys	Gly Ser Arg Gly Gly	Arg Lys Gly Gly Pro	Pro		
	365		370		375
Phe Thr Gln Glu	Glu Glu Glu Asp Gly	Gly Pro Ala Leu Gln	Glu		
	380		385		390
Leu Leu Ser Thr	Arg Pro Thr Gly Ser	Val Ser Ser Thr Leu	Gly		
	395		400		405
Leu Ala Ser Ile	Gln Pro Ser Lys Val	Gly Lys Lys Lys Lys	Val		
	410		415		420
Gly Ser Glu Lys	Pro Gly Thr Thr Leu	Pro Gln Pro Pro Pro	Ala		
	425		430		435
Thr Cys Pro Pro	Gly Ala Leu Gln Ala	Pro Glu Ala Pro Ala	Ser		
	440		445		450
Arg Ala Glu Gly	Pro Val Ala Val Val	Val Asn Gly His Thr	Glu		
	455		460		465
Gly Pro Ala Pro	Ala Arg Ser Ala Pro	Lys Glu Pro Pro Gly	Leu		
	470		475		480
Pro Arg Pro Leu	Gly Ser Phe Pro Cys	Pro Thr Pro Gln Glu	Asp		
	485		490		495
Phe Pro Ala Leu	Gly Gly Pro Cys Pro	Pro Arg Met Pro Pro	Pro		
	500		505		510
Pro Gly Phe Ser	Ala Val Val Leu Leu	Lys Gly Thr Pro Pro	Pro		
	515		520		525
Pro Pro Pro Gly	Leu Val Pro Pro Ile	Ser Lys Pro Pro Pro	Gly		
	530		535		540
Phe Ser Gly Leu	Leu Pro Ser Pro His	Pro Ala Ser Val Pro	Ser		
	545		550		555
Pro Ala Thr Thr	Thr Thr Thr Lys Ala	Pro Arg Leu Leu Pro	Ala		
	560		565		570
Pro Arg Ala Tyr	Leu Val Pro Glu Asn	Phe Arg Glu Arg Asn	Leu		
	575		580		585
Gln Leu Ile Gln	Ser Ile Arg Asp Phe	Leu Gln Ser Asp Glu	Ala		
	590		595		600
Arg Phe Ser Glu	Phe Lys Ser His Ser	Gly Glu Phe Arg Gln	Gly		
	605		610		615
Leu Ile Ser Ala	Ala Gln Tyr Tyr Lys	Ser Cys Arg Asp Leu	Leu		
	620		625		630
Gly Glu Asn Phe	Gln Lys Val Phe Asn	Glu Leu Leu Val Leu	Leu		
	635		640		645
Pro Asp Thr Ala	Lys Gln Gln Glu Leu	Leu Ser Ala His Thr	Asp		
	650		655		660

Phe	Cys	Asn	Arg	Glu	Lys	Pro	Leu	Ser	Thr	Lys	Ser	Lys	Lys	Asn
				665					670					675
Lys	Lys	Ser	Ala	Trp	Gln	Ala	Thr	Thr	Gln	Gln	Ala	Gly	Leu	Asp
				680					685					690
Cys	Arg	Val	Cys	Pro	Thr	Cys	Gln	Gln	Val	Leu	Ala	His	Gly	Asp
				695					700					705
Ala	Ser	Ser	His	Gln	Ala	Leu	His	Ala	Ala	Arg	Asp	Asp	Asp	Phe
				710					715					720
Pro	Ser	Leu	Gln	Ala	Ile	Ala	Arg	Ile	Ile	Thr				
				725					730					

<210> 16  
 <211> 299  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte ID No: 1748508CD1

<400> 16

Met	Glu	Thr	Tyr	Phe	Val	Glu	Ile	Ile	Leu	Cys	Lys	Tyr	Val	Phe
1				5					10					15
Asn	Thr	Tyr	Phe	Ile	Phe	Leu	Thr	Phe	Gln	Asn	Tyr	His	Glu	Ile
				20					25					30
Met	Thr	Arg	His	Pro	Glu	Asn	Tyr	Gln	Trp	Glu	Asn	Trp	Ser	Leu
				35					40					45
Glu	Asn	Val	Ala	Thr	Ile	Leu	Ala	His	Arg	Phe	Pro	Asn	Ser	Tyr
				50					55					60
Ile	Trp	Val	Ile	Lys	Cys	Ser	Arg	Met	His	Leu	His	Lys	Phe	Ser
				65					70					75
Cys	Tyr	Asp	Asn	Phe	Val	Lys	Ser	Asn	Met	Phe	Gly	Ala	Pro	Glu
				80					85					90
His	Asn	Thr	Asp	Phe	Gly	Ala	Phe	Lys	His	Leu	Tyr	Met	Leu	Leu
				95					100					105
Val	Asn	Ala	Phe	Asn	Leu	Ser	Gln	Asn	Ser	Leu	Ser	Lys	Lys	Ser
				110					115					120
Leu	Asn	Val	Trp	Asn	Lys	Asp	Ser	Ile	Ala	Ser	Asn	Cys	Arg	Ser
				125					130					135
Ser	Pro	Ser	His	Thr	Asn	Gly	Cys	Gln	Gly	Glu	Lys	Val	Arg	
				140					145					150
Thr	Cys	Glu	Lys	Ser	Asp	Glu	Ser	Ala	Met	Ser	Phe	Tyr	Pro	Pro
				155					160					165
Ser	Leu	Asn	Asp	Ala	Ser	Phe	Thr	Leu	Ile	Gly	Phe	Ser	Lys	Gly
				170					175					180
Cys	Val	Val	Leu	Asn	Gln	Leu	Leu	Phe	Glu	Leu	Lys	Glu	Ala	Lys
				185					190					195
Lys	Asp	Lys	Asn	Ile	Asp	Ala	Phe	Ile	Lys	Ser	Ile	Arg	Thr	Met
				200					205					210
Tyr	Trp	Leu	Asp	Gly	Gly	His	Ser	Gly	Gly	Ser	Asn	Thr	Trp	Val
				215					220					225
Thr	Tyr	Pro	Glu	Val	Leu	Lys	Glu	Phe	Ala	Gln	Thr	Gly	Ile	Ile
				230					235					240
Val	His	Thr	His	Val	Thr	Pro	Tyr	Gln	Val	Arg	Asp	Pro	Met	Arg
				245					250					255
Ser	Trp	Ile	Gly	Lys	Glu	His	Lys	Lys	Phe	Val	Gln	Ile	Leu	Gly
				260					265					270
Asp	Leu	Gly	Met	Gln	Val	Thr	Ser	Gln	Ile	His	Phe	Thr	Lys	Glu
				275					280					285
Ala	Pro	Ser	Ile	Glu	Asn	His	Phe	Arg	Val	His	Glu	Val	Phe	
				290					295					

<210> 17

<211> 620  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte ID No: 2159545CD1

<400> 17

Met	Ala	Ser	Asp	Ser	Met	Ser	Ser	Lys	Gln	Ala	Arg	Asn	His	Ile	1	5	10	15
Thr	Lys	Gly	Lys	Arg	Gln	Gln	Gln	His	Gln	Gln	Ile	Lys	Asn	Arg	20	25	30	35
Ser	Ser	Ile	Ser	Asp	Gly	Asp	Gly	Glu	Asp	Ser	Phe	Ile	Phe	Glu	40	45	50	55
Ala	Asn	Glu	Ala	Trp	Lys	Asp	Phe	His	Gly	Ser	Leu	Leu	Arg	Phe	60	65	70	75
Tyr	Glu	Asn	Gly	Glu	Leu	Cys	Asp	Val	Thr	Leu	Lys	Val	Gly	Ser	80	85	90	95
Lys	Leu	Ile	Ser	Cys	His	Lys	Leu	Val	Leu	Ala	Cys	Val	Ile	Pro	100	105	110	115
Tyr	Phe	Arg	Ala	Met	Phe	Leu	Ser	Glu	Met	Ala	Glu	Ala	Lys	Gln	120	125	130	135
Thr	Leu	Ile	Glu	Ile	Arg	Asp	Phe	Asp	Gly	Asp	Ala	Ile	Glu	Asp	140	145	150	155
Leu	Val	Lys	Phe	Val	Tyr	Ser	Ser	Arg	Leu	Thr	Leu	Thr	Val	Asp	160	165	170	175
Asn	Val	Gln	Pro	Leu	Leu	Tyr	Ala	Ala	Cys	Ile	Leu	Gln	Val	Glu	180	185	190	195
Leu	Val	Ala	Arg	Ala	Cys	Cys	Glu	Tyr	Met	Lys	Leu	His	Phe	His	200	205	210	215
Pro	Ser	Asn	Cys	Leu	Ala	Val	Arg	Ala	Phe	Ala	Glu	Ser	His	Asn	220	225	230	235
Arg	Ile	Asp	Leu	Met	Asp	Met	Ala	Asp	Gln	Tyr	Ala	Cys	Asp	His	240	245	250	255
Phe	Thr	Glu	Val	Val	Glu	Cys	Glu	Asp	Phe	Val	Ser	Val	Ser	Pro	260	265	270	275
Gln	His	Leu	His	Lys	Leu	Leu	Ser	Ser	Ser	Asp	Leu	Asn	Ile	Glu	280	285	290	295
Asn	Glu	Lys	Gln	Val	Tyr	Asn	Ala	Ala	Ile	Lys	Trp	Leu	Leu	Ala	300	305	310	315
Asn	Pro	Gln	His	His	Ser	Lys	Trp	Leu	Asp	Glu	Thr	Leu	Ala	Gln	320	325	330	335
Val	Arg	Leu	Pro	Leu	Leu	Pro	Val	Asp	Phe	Leu	Met	Gly	Val	Val	340	345	350	355
Ala	Lys	Glu	Gln	Ile	Val	Lys	Gln	Asn	Leu	Lys	Cys	Arg	Asp	Leu	360	365	370	375
Leu	Asp	Glu	Ala	Arg	Asn	Tyr	His	Leu	His	Leu	Ser	Ser	Arg	Ala	380	385	390	395
Val	Pro	Asp	Phe	Glu	Tyr	Ser	Ile	Arg	Thr	Thr	Pro	Arg	Lys	His	400			
Thr	Ala	Gly	Val	Leu	Phe	Cys	Val	Gly	Gly	Arg	Gly	Gly	Ser	Gly				
Asp	Pro	Phe	Arg	Ser	Ile	Glu	Cys	Tyr	Ser	Ile	Asn	Lys	Asn	Ser				
Trp	Phe	Phe	Gly	Pro	Glu	Met	Asn	Ser	Arg	Arg	Arg	His	Val	Gly				
Val	Ile	Ser	Val	Glu	Gly	Lys	Val	Tyr	Ala	Val	Gly	Gly	His	Asp				
Gly	Asn	Glu	His	Leu	Gly	Ser	Met	Glu	Met	Phe	Asp	Pro	Leu	Thr				
Asn	Lys	Trp	Met	Met	Lys	Ala	Ser	Met	Asn	Thr	Lys	Arg	Arg	Gly				

Ile	Ala	Leu	Ala	Ser	Leu	Gly	Gly	Pro	Ile	Tyr	Ala	Ile	Gly	Gly	
				410					415					420	
Leu	Asp	Asp	Asn	Thr	Cys	Phe	Asn	Asp	Val	Glu	Arg	Tyr	Asp	Ile	
				425					430					435	
Glu	Ser	Asp	Gln	Trp	Ser	Thr	Val	Ala	Pro	Met	Asn	Thr	Pro	Arg	
				440					445					450	
Gly	Gly	Val	Gly	Ser	Val	Ala	Leu	Val	Asn	His	Val	Tyr	Ala	Val	
				455					460					465	
Gly	Gly	Asn	Asp	Gly	Met	Ala	Ser	Leu	Ser	Ser	Val	Glu	Arg	Tyr	
				470					475					480	
Asp	Pro	His	Leu	Asp	Lys	Trp	Ile	Glu	Val	Lys	Glu	Met	Gly	Gln	
				485					490					495	
Arg	Arg	Ala	Gly	Asn	Gly	Val	Ser	Lys	Leu	His	Gly	Cys	Leu	Tyr	
				500					505					510	
Val	Val	Gly	Gly	Phe	Asp	Asp	Asn	Ser	Pro	Leu	Ser	Ser	Val	Glu	
				515					520					525	
Arg	Tyr	Asp	Pro	Arg	Ser	Asn	Lys	Trp	Asp	Tyr	Val	Ala	Ala	Leu	
				530					535					540	
Thr	Thr	Pro	Arg	Gly	Gly	Val	Gly	Ile	Ala	Thr	Val	Met	Gly	Lys	
				545					550					555	
Ile	Phe	Ala	Val	Gly	Gly	His	Asn	Gly	Asn	Ala	Tyr	Leu	Asn	Thr	
				560					565					570	
Val	Glu	Ala	Phe	Asp	Pro	Val	Leu	Asn	Arg	Trp	Glu	Leu	Val	Gly	
				575					580					585	
Ser	Val	Ser	His	Cys	Arg	Ala	Gly	Ala	Gly	Val	Ala	Val	Cys	Ser	
				590					595					600	
Cys	Leu	Thr	Ser	Gln	Ile	Arg	Asp	Val	Gly	His	Gly	Ser	Asn	Asn	
				605					610					615	
Val	Val	Asp	Cys	Met											
				620											

&lt;210&gt; 18

&lt;211&gt; 218

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte ID No: 8560269CD1

&lt;400&gt; 18

Met	Ala	Leu	Val	Pro	Tyr	Glu	Glu	Thr	Thr	Glu	Phe	Gly	Leu	Gln	
1				5					10					15	
Lys	Phe	His	Lys	Pro	Leu	Ala	Thr	Phe	Ser	Phe	Ala	Asn	His	Thr	
				20					25					30	
Ile	Gln	Ile	Arg	Gln	Asp	Trp	Arg	His	Leu	Gly	Val	Ala	Ala	Val	
				35					40					45	
Val	Trp	Asp	Ala	Ala	Ile	Val	Leu	Ser	Thr	Tyr	Leu	Glu	Met	Gly	
				50					55					60	
Ala	Val	Glu	Leu	Arg	Gly	Arg	Ser	Ala	Val	Glu	Leu	Gly	Ala	Gly	
				65					70					75	
Thr	Gly	Leu	Val	Gly	Ile	Val	Ala	Ala	Leu	Leu	Gly	Ala	His	Val	
				80					85					90	
Thr	Ile	Thr	Asp	Arg	Lys	Val	Ala	Leu	Glu	Phe	Leu	Lys	Ser	Asn	
				95					100					105	
Val	Gln	Ala	Asn	Leu	Pro	Pro	His	Ile	Gln	Thr	Lys	Thr	Val	Val	
				110					115					120	
Lys	Glu	Leu	Thr	Trp	Gly	Gln	Asn	Leu	Gly	Ser	Phe	Ser	Pro	Gly	
				125					130					135	
Glu	Phe	Asp	Leu	Ile	Leu	Gly	Ala	Asp	Ile	Ile	Tyr	Leu	Glu	Glu	
				140					145					150	
Thr	Phe	Thr	Asp	Leu	Leu	Gln	Thr	Leu	Glu	His	Leu	Cys	Ser	Asn	
				155					160					165	

His	Ser	Val	Ile	Leu	Leu	Ala	Cys	Arg	Ile	Arg	Tyr	Glu	Arg	Asp	
				170					175					180	
Asn	Asn	Phe	Leu	Ala	Met	Leu	Glu	Arg	Gln	Phe	Ile	Val	Arg	Lys	
				185					190					195	
Val	His	Tyr	Asp	Pro	Glu	Lys	Asp	Val	His	Ile	Tyr	Glu	Ala	Gln	
				200					205					210	
Lys	Arg	Asn	Gln	Lys	Glu	Asp	Leu								
				215											

&lt;210&gt; 19

&lt;211&gt; 427

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte ID No: 8710302CD1

&lt;400&gt; 19

Met	Ala	Ala	Leu	Ser	Lys	Ser	Ile	Pro	His	Asn	Cys	Tyr	Glu	Ile	
1				5					10					15	
Gly	His	Thr	Trp	His	Pro	Ser	Cys	Arg	Val	Ser	Phe	Leu	Gln	Ile	
				20					25					30	
Thr	Gly	Gly	Ala	Leu	Glu	Glu	Ser	Leu	Lys	Ile	Tyr	Ala	Pro	Leu	
				35					40					45	
Tyr	Leu	Ile	Ala	Ala	Ile	Leu	Arg	Lys	Arg	Lys	Leu	Asp	Tyr	Tyr	
				50					55					60	
Leu	His	Lys	Leu	Leu	Pro	Glu	Ile	Leu	Gln	Ser	Ala	Ser	Phe	Leu	
				65					70					75	
Thr	Ala	Asn	Gly	Ala	Leu	Tyr	Met	Ala	Phe	Phe	Cys	Ile	Leu	Arg	
				80					85					90	
Arg	Gly	Leu	Leu	Thr	Ile	Tyr	Met	Ala	Asn	Leu	Ala	Thr	Glu	Thr	
				95					100					105	
Leu	Phe	Arg	Met	Gly	Val	Ala	Arg	Gly	Thr	Ile	Thr	Thr	Leu	Arg	
				110					115					120	
Asn	Gly	Glu	Val	Leu	Leu	Phe	Cys	Ile	Thr	Ala	Ala	Met	Tyr	Met	
				125					130					135	
Phe	Phe	Phe	Arg	Cys	Lys	Asp	Gly	Leu	Lys	Gly	Phe	Thr	Phe	Ser	
				140					145					150	
Ala	Leu	Arg	Phe	Ile	Val	Gly	Lys	Glu	Glu	Ile	Pro	Thr	His	Ser	
				155					160					165	
Phe	Ser	Pro	Glu	Ala	Ala	Tyr	Ala	Lys	Val	Glu	Gln	Lys	Arg	Glu	
				170					175					180	
Gln	His	Glu	Glu	Lys	Pro	Arg	Arg	Met	Asn	Met	Ile	Gly	Leu	Val	
				185					190					195	
Arg	Lys	Phe	Val	Asp	Ser	Ile	Cys	Lys	His	Gly	Pro	Arg	His	Arg	
				200					205					210	
Cys	Cys	Lys	His	Tyr	Glu	Asp	Asn	Cys	Ile	Ser	Tyr	Cys	Ile	Lys	
				215					220					225	
Gly	Phe	Ile	Arg	Met	Phe	Ser	Val	Gly	Tyr	Leu	Ile	Gln	Cys	Cys	
				230					235					240	
Leu	Arg	Ile	Pro	Ser	Ala	Phe	Arg	His	Leu	Phe	Thr	Gln	Pro	Ser	
				245					250					255	
Arg	Leu	Leu	Ser	Leu	Phe	Tyr	Asn	Lys	Glu	Asn	Phe	Gln	Leu	Gly	
				260					265					270	
Ala	Phe	Leu	Gly	Ser	Phe	Val	Ser	Ile	Tyr	Lys	Gly	Thr	Ser	Cys	
				275					280					285	
Phe	Leu	Arg	Trp	Ile	Arg	Asn	Leu	Asp	Asp	Glu	Leu	His	Ala	Ile	
				290					295					300	
Ile	Ala	Gly	Phe	Leu	Ala	Gly	Ile	Ser	Met	Met	Phe	Tyr	Lys	Ser	
				305					310					315	
Thr	Thr	Ile	Ser	Met	Tyr	Leu	Ala	Ser	Lys	Leu	Val	Glu	Thr	Met	
				320					325					330	



Tyr	Phe	Lys	Gly	Ile	Glu	Ala	Gly	Lys	Val	Pro	Tyr	Phe	Pro	His
				335					340					345
Ala	Asp	Thr	Ile	Ile	Tyr	Ser	Ile	Ser	Thr	Ala	Ile	Cys	Phe	Gln
				350					355					360
Ala	Ala	Val	Met	Glu	Val	Gln	Thr	Leu	Arg	Pro	Ser	Tyr	Trp	Lys
				365					370					375
Phe	Leu	Leu	Arg	Leu	Thr	Lys	Gly	Lys	Phe	Ala	Val	Met	Asn	Arg
				380					385					390
Lys	Val	Leu	Asp	Val	Phe	Gly	Thr	Gly	Ala	Ser	Lys	His	Phe	Gln
				395					400					405
Asp	Phe	Ile	Pro	Arg	Leu	Asp	Pro	Arg	Tyr	Thr	Thr	Val	Thr	Pro
				410					415					420
Glu	Leu	Pro	Thr	Glu	Phe	Ser								
				425										

&lt;210&gt; 20

&lt;211&gt; 612

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte ID No: 6778214CD1

&lt;400&gt; 20

Met	Glu	Ile	Ala	Pro	Gln	Glu	Ala	Pro	Pro	Val	Pro	Gly	Ala	Asp
1				5					10					15
Gly	Asp	Ile	Glu	Glu	Ala	Pro	Ala	Glu	Ala	Gly	Ser	Pro	Ser	Pro
				20					25					30
Ala	Ser	Pro	Pro	Ala	Asp	Gly	Arg	Leu	Lys	Ala	Ala	Ala	Lys	Arg
				35					40					45
Val	Thr	Phe	Pro	Ser	Asp	Glu	Asp	Ile	Val	Ser	Gly	Ala	Val	Glu
				50					55					60
Pro	Lys	Asp	Pro	Trp	Arg	His	Ala	Gln	Asn	Val	Thr	Val	Asp	Glu
				65					70					75
Val	Ile	Gly	Ala	Tyr	Lys	Gln	Ala	Cys	Gln	Lys	Leu	Asn	Cys	Arg
				80					85					90
Gln	Ile	Pro	Lys	Leu	Leu	Arg	Gln	Leu	Gln	Glu	Phe	Thr	Asp	Leu
				95					100					105
Gly	His	Arg	Leu	Asp	Cys	Leu	Asp	Leu	Lys	Gly	Glu	Lys	Leu	Asp
				110					115					120
Tyr	Lys	Thr	Cys	Glu	Ala	Leu	Glu	Glu	Val	Phe	Lys	Arg	Leu	Gln
				125					130					135
Phe	Lys	Val	Val	Asp	Leu	Glu	Gln	Thr	Asn	Leu	Asp	Glu	Asp	Gly
				140					145					150
Ala	Ser	Ala	Leu	Phe	Asp	Met	Ile	Glu	Tyr	Tyr	Glu	Ser	Ala	Thr
				155					160					165
His	Leu	Asn	Ile	Ser	Phe	Asn	Lys	His	Ile	Gly	Thr	Arg	Gly	Trp
				170					175					180
Gln	Ala	Ala	Ala	His	Met	Met	Arg	Lys	Thr	Ser	Cys	Leu	Gln	Tyr
				185					190					195
Leu	Asp	Ala	Arg	Asn	Thr	Pro	Leu	Leu	Asp	His	Ser	Ala	Pro	Phe
				200					205					210
Val	Ala	Arg	Ala	Leu	Arg	Ile	Arg	Ser	Ser	Leu	Ala	Val	Leu	His
				215					220					225
Leu	Glu	Asn	Ala	Ser	Leu	Ser	Gly	Arg	Pro	Leu	Met	Leu	Leu	Ala
				230					235					240
Thr	Ala	Leu	Lys	Met	Asn	Met	Asn	Leu	Arg	Glu	Leu	Tyr	Leu	Ala
				245					250					255
Asp	Asn	Lys	Leu	Asn	Gly	Leu	Gln	Asp	Ser	Ala	Gln	Leu	Gly	Asn
				260					265					270
Leu	Leu	Lys	Phe	Asn	Cys	Ser	Leu	Gln	Ile	Leu	Asp	Leu	Arg	Asn
				275					280					285

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Asn His Val Leu Asp Ser Gly Leu Ala Tyr Ile Cys Glu Gly Leu
290 295 300
Lys Glu Gln Arg Lys Gly Leu Val Thr Leu Val Leu Trp Asn Asn
305 310 315
Gln Leu Thr His Thr Gly Met Ala Phe Leu Gly Met Thr Leu Pro
320 325 330
His Thr Gln Ser Leu Glu Thr Leu Asn Leu Gly His Asn Pro Ile
335 340 345
Gly Asn Glu Gly Val Arg His Leu Lys Asn Gly Leu Ile Ser Asn
350 355 360
Arg Ser Val Leu Arg Leu Gly Leu Ala Ser Thr Lys Leu Thr Cys
365 370 375
Glu Gly Ala Val Ala Val Ala Glu Phe Ile Ala Glu Ser Pro Arg
380 385 390
Leu Leu Arg Leu Asp Leu Arg Glu Asn Glu Ile Lys Thr Gly Gly
395 400 405
Leu Met Ala Leu Ser Leu Ala Leu Lys Val Asn His Ser Leu Leu
410 415 420
Arg Leu Asp Leu Asp Arg Glu Pro Lys Lys Glu Ala Val Lys Ser
425 430 435
Phe Ile Glu Thr Gln Lys Ala Leu Leu Ala Glu Ile Gln Asn Gly
440 445 450
Cys Lys Arg Asn Leu Val Leu Ala Arg Glu Arg Glu Glu Lys Glu
455 460 465
Gln Pro Pro Gln Leu Ser Ala Ser Met Pro Glu Thr Thr Ala Thr
470 475 480
Glu Pro Gln Pro Asp Asp Glu Pro Ala Ala Gly Val Gln Asn Gly
485 490 495
Ala Pro Ser Pro Ala Pro Ser Pro Asp Ser Asp Ser Asp Ser Asp
500 505 510
Ser Asp Gly Glu Glu Glu Glu Glu Glu Glu Gly Glu Arg Asp Glu
515 520 525
Thr Pro Ser Gly Ala Ile Asp Thr Arg Asp Thr Gly Ser Ser Glu
530 535 540
Pro Gln Pro Pro Pro Glu Pro Pro Arg Ser Gly Pro Pro Leu Pro
545 550 555
Asn Gly Leu Lys Pro Glu Phe Ala Leu Ala Leu Pro Pro Glu Pro
560 565 570
Pro Pro Gly Pro Glu Val Lys Gly Gly Ser Cys Gly Leu Glu His
575 580 585
Glu Leu Ser Cys Ser Lys Asn Glu Lys Glu Leu Glu Glu Leu Leu
590 595 600
Leu Glu Ala Ser Gln Glu Ser Gly Gln Glu Thr Leu
605 610

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&lt;210&gt; 21

&lt;211&gt; 458

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte ID No: 258383CD1

&lt;400&gt; 21

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Met Ala Ala Leu Ser Lys Ser Ile Pro His Asn Cys Tyr Glu Ile
1 5 10 15
Gly His Thr Trp His Pro Ser Cys Arg Val Ser Phe Leu Gln Ile
20 25 30
Thr Gly Gly Ala Leu Glu Glu Ser Leu Lys Ile Tyr Ala Pro Leu
35 40 45
Tyr Leu Ile Ala Ala Ile Leu Arg Lys Arg Lys Leu Asp Tyr Tyr
50 55 60

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Leu	His	Lys	Leu	Leu	Pro	Glu	Ile	Leu	Gln	Ser	Ala	Ser	Phe	Leu	
				65					70					75	
Thr	Ala	Asn	Gly	Ala	Leu	Tyr	Met	Ala	Phe	Phe	Cys	Ile	Leu	Arg	
				80					85					90	
Lys	Ile	Leu	Gly	Lys	Phe	Tyr	Ser	Trp	Thr	Pro	Gly	Phe	Gly	Ala	
				95					100					105	
Ala	Leu	Pro	Ala	Ser	Tyr	Val	Ala	Ile	Leu	Ile	Glu	Arg	Lys	Ser	
				110					115					120	
Arg	Arg	Gly	Leu	Leu	Thr	Ile	Tyr	Met	Ala	Asn	Leu	Ala	Thr	Glu	
				125					130					135	
Thr	Leu	Phe	Arg	Met	Gly	Val	Ala	Arg	Gly	Thr	Ile	Thr	Thr	Leu	
				140					145					150	
Arg	Asn	Gly	Glu	Val	Leu	Leu	Phe	Cys	Ile	Thr	Ala	Ala	Met	Tyr	
				155					160					165	
Met	Phe	Phe	Phe	Arg	Cys	Lys	Asp	Gly	Leu	Lys	Gly	Phe	Thr	Phe	
				170					175					180	
Ser	Ala	Leu	Arg	Phe	Ile	Val	Gly	Lys	Glu	Glu	Ile	Pro	Thr	His	
				185					190					195	
Ser	Phe	Ser	Pro	Glu	Ala	Ala	Tyr	Ala	Lys	Val	Glu	Gln	Lys	Arg	
				200					205					210	
Glu	Gln	His	Glu	Glu	Lys	Pro	Arg	Arg	Met	Asn	Met	Ile	Gly	Leu	
				215					220					225	
Val	Arg	Lys	Phe	Val	Asp	Ser	Ile	Cys	Lys	His	Gly	Pro	Arg	His	
				230					235					240	
Arg	Cys	Cys	Lys	His	Tyr	Glu	Asp	Asn	Cys	Ile	Ser	Tyr	Cys	Ile	
				245					250					255	
Lys	Gly	Phe	Ile	Arg	Met	Phe	Ser	Val	Gly	Tyr	Leu	Ile	Gln	Cys	
				260					265					270	
Cys	Leu	Arg	Ile	Pro	Ser	Ala	Phe	Arg	His	Leu	Phe	Thr	Gln	Pro	
				275					280					285	
Ser	Arg	Leu	Leu	Ser	Leu	Phe	Tyr	Asn	Lys	Glu	Asn	Phe	Gln	Leu	
				290					295					300	
Gly	Ala	Phe	Leu	Gly	Ser	Phe	Val	Ser	Ile	Tyr	Lys	Gly	Thr	Ser	
				305					310					315	
Cys	Phe	Leu	Arg	Trp	Ile	Arg	Asn	Leu	Asp	Asp	Glu	Leu	His	Ala	
				320					325					330	
Ile	Ile	Ala	Gly	Phe	Leu	Ala	Gly	Ile	Ser	Met	Met	Phe	Tyr	Lys	
				335					340					345	
Ser	Thr	Thr	Ile	Ser	Met	Tyr	Leu	Ala	Ser	Lys	Leu	Val	Glu	Thr	
				350					355					360	
Met	Tyr	Phe	Lys	Gly	Ile	Glu	Ala	Gly	Lys	Val	Pro	Tyr	Phe	Pro	
				365					370					375	
His	Ala	Asp	Thr	Ile	Ile	Tyr	Ser	Ile	Ser	Thr	Ala	Ile	Cys	Phe	
				380					385					390	
Gln	Ala	Ala	Val	Met	Glu	Val	Gln	Thr	Leu	Arg	Pro	Ser	Tyr	Trp	
				395					400					405	
Lys	Phe	Leu	Leu	Arg	Leu	Thr	Lys	Gly	Lys	Phe	Ala	Val	Met	Asn	
				410					415					420	
Arg	Lys	Val	Leu	Asp	Val	Phe	Gly	Thr	Gly	Ala	Ser	Lys	His	Phe	
				425					430					435	
Gln	Asp	Phe	Ile	Pro	Arg	Leu	Asp	Pro	Arg	Tyr	Thr	Thr	Val	Thr	
				440					445					450	
Pro	Glu	Leu	Pro	Thr	Glu	Phe	Ser								
				455											

&lt;210&gt; 22

&lt;211&gt; 1451

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte ID No: 2804937CD1

&lt;400&gt; 22

Met	Ser	Leu	Val	Asn	Phe	Glu	Pro	Ala	Ala	Arg	Arg	Ala	Ser	Asn
1				5					10					15
Ile	Cys	Asp	Thr	Asp	Ser	His	Val	Ser	Ser	Ser	Thr	Ser	Val	Arg
				20					25					30
Phe	Tyr	Pro	His	Asp	Val	Leu	Ser	Leu	Pro	Gln	Ile	Arg	Leu	Asn
				35					40					45
Arg	Leu	Leu	Thr	Ile	Asp	Thr	Asp	Leu	Leu	Glu	Gln	Gln	Asp	Ile
				50					55					60
Asp	Leu	Ser	Pro	Asp	Leu	Ala	Ala	Thr	Tyr	Gly	Pro	Thr	Glu	Glu
				65					70					75
Ala	Ala	Gln	Lys	Val	Lys	His	Tyr	Tyr	Arg	Phe	Trp	Ile	Leu	Pro
				80					85					90
Gln	Leu	Trp	Ile	Gly	Ile	Asn	Phe	Asp	Arg	Leu	Thr	Leu	Leu	Ala
				95					100					105
Leu	Phe	Asp	Arg	Asn	Arg	Glu	Ile	Leu	Glu	Asn	Val	Leu	Ala	Val
				110					115					120
Ile	Leu	Ala	Ile	Leu	Val	Ala	Phe	Leu	Gly	Ser	Ile	Leu	Leu	Ile
				125					130					135
Gln	Gly	Phe	Phe	Arg	Asp	Ile	Trp	Val	Phe	Gln	Phe	Cys	Leu	Val
				140					145					150
Ile	Ala	Ser	Cys	Gln	Tyr	Ser	Leu	Leu	Lys	Ser	Val	Gln	Pro	Asp
				155					160					165
Ser	Ser	Ser	Pro	Arg	His	Gly	His	Asn	Arg	Ile	Ile	Ala	Tyr	Ser
				170					175					180
Arg	Pro	Val	Tyr	Phe	Cys	Ile	Cys	Cys	Gly	Leu	Ile	Trp	Leu	Leu
				185					190					195
Asp	Tyr	Gly	Ser	Arg	Asn	Leu	Thr	Ala	Thr	Lys	Phe	Lys	Leu	Tyr
				200					205					210
Gly	Ile	Thr	Phe	Thr	Asn	Pro	Leu	Val	Phe	Ile	Ser	Ala	Arg	Asp
				215					220					225
Leu	Val	Ile	Val	Phe	Thr	Leu	Cys	Phe	Pro	Ile	Val	Phe	Phe	Ile
				230					235					240
Gly	Leu	Leu	Pro	Gln	Val	Asn	Thr	Phe	Val	Met	Tyr	Leu	Cys	Glu
				245					250					255
Gln	Leu	Asp	Ile	His	Ile	Phe	Gly	Gly	Asn	Ala	Thr	Thr	Ser	Leu
				260					265					270
Leu	Ala	Ala	Leu	Tyr	Ser	Phe	Ile	Cys	Ser	Ile	Val	Ala	Val	Ala
				275					280					285
Leu	Leu	Tyr	Gly	Leu	Cys	Tyr	Gly	Ala	Leu	Lys	Asp	Ser	Trp	Asp
				290					295					300
Gly	Gln	His	Ile	Pro	Val	Leu	Phe	Ser	Ile	Phe	Cys	Gly	Leu	Leu
				305					310					315
Val	Ala	Val	Ser	Tyr	His	Leu	Ser	Arg	Gln	Ser	Ser	Asp	Pro	Ser
				320					325					330
Val	Leu	Phe	Ser	Leu	Val	Gln	Ser	Lys	Ile	Phe	Pro	Lys	Thr	Glu
				335					340					345
Glu	Lys	Asn	Pro	Glu	Asp	Pro	Leu	Ser	Glu	Val	Lys	Asp	Pro	Leu
				350					355					360
Pro	Glu	Lys	Leu	Arg	Asn	Ser	Val	Ser	Glu	Arg	Leu	Gln	Ser	Asp
				365					370					375
Leu	Val	Val	Cys	Ile	Val	Ile	Gly	Val	Leu	Tyr	Phe	Ala	Ile	His
				380					385					390
Val	Ser	Thr	Val	Phe	Thr	Val	Leu	Gln	Pro	Ala	Leu	Lys	Tyr	Val
				395					400					405
Leu	Tyr	Thr	Leu	Val	Gly	Phe	Val	Gly	Phe	Val	Thr	His	Tyr	Val
				410					415					420
Leu	Pro	Gln	Val	Arg	Lys	Gln	Leu	Pro	Trp	His	Cys	Phe	Ser	His
				425					430					435
Pro	Leu	Leu	Lys	Thr	Leu	Glu	Tyr	Asn	Gln	Tyr	Glu	Val	Arg	Asn
				440					445					450
Ala	Ala	Thr	Met	Met	Trp	Phe	Glu	Lys	Leu	His	Val	Trp	Leu	Leu
				455					460					465

Phe Val Glu Lys Asn Ile Ile Tyr Pro Leu Ile Val Leu Asn Glu		
470	475	480
Leu Ser Ser Ser Ala Glu Thr Ile Ala Ser Pro Lys Lys Leu Asn		
485	490	495
Thr Glu Leu Gly Ala Leu Met Ile Thr Val Ala Gly Leu Lys Leu		
500	505	510
Leu Arg Ser Ser Phe Ser Ser Pro Thr Tyr Gln Tyr Val Thr Val		
515	520	525
Ile Phe Thr Val Leu Phe Phe Lys Phe Asp Tyr Glu Ala Phe Ser		
530	535	540
Glu Thr Met Leu Leu Asp Leu Phe Phe Met Ser Ile Leu Phe Asn		
545	550	555
Lys Leu Trp Glu Leu Leu Tyr Lys Leu Gln Phe Val Tyr Thr Tyr		
560	565	570
Ile Ala Pro Trp Gln Ile Thr Trp Gly Ser Ala Phe His Ala Phe		
575	580	585
Ala Gln Pro Phe Ala Val Pro His Ser Ala Met Leu Phe Ile Gln		
590	595	600
Ala Ala Val Ser Ala Phe Phe Ser Thr Pro Leu Asn Pro Phe Leu		
605	610	615
Gly Ser Ala Ile Phe Ile Thr Ser Tyr Val Arg Pro Val Lys Phe		
620	625	630
Trp Glu Arg Asp Tyr Asn Thr Lys Arg Val Asp His Ser Asn Thr		
635	640	645
Arg Leu Ala Ser Gln Leu Asp Arg Asn Pro Gly Ser Asp Asp Asn		
650	655	660
Asn Leu Asn Ser Ile Phe Tyr Glu His Leu Thr Arg Ser Leu Gln		
665	670	675
His Ser Leu Cys Gly Asp Leu Leu Leu Gly Arg Trp Gly Asn Tyr		
680	685	690
Ser Thr Gly Asp Cys Phe Ile Leu Ala Ser Asp Tyr Leu Asn Ala		
695	700	705
Leu Val His Leu Ile Glu Ile Gly Asn Gly Leu Val Thr Phe Gln		
710	715	720
Leu Arg Gly Leu Glu Phe Arg Gly Thr Tyr Cys Gln Gln Arg Glu		
725	730	735
Val Glu Ala Ile Thr Glu Gly Val Glu Glu Asp Glu Gly Phe Cys		
740	745	750
Cys Cys Glu Pro Gly His Ile Pro His Met Leu Ser Phe Asn Ala		
755	760	765
Ala Phe Ser Gln Arg Trp Leu Ala Trp Glu Val Ile Val Thr Lys		
770	775	780
Tyr Ile Leu Glu Gly Tyr Ser Ile Thr Asp Asn Ser Ala Ala Ser		
785	790	795
Met Leu Gln Val Phe Asp Leu Arg Lys Val Leu Thr Thr Tyr Tyr		
800	805	810
Val Lys Gly Ile Ile Tyr Tyr Val Thr Thr Ser Ser Lys Leu Glu		
815	820	825
Glu Trp Leu Ala Asn Glu Thr Met Gln Glu Gly Leu Arg Leu Cys		
830	835	840
Ala Asp Arg Asn Tyr Val Asp Val Asp Pro Thr Phe Asn Pro Asn		
845	850	855
Ile Asp Glu Asp Tyr Asp His Arg Leu Ala Gly Ile Ser Arg Glu		
860	865	870
Ser Phe Cys Val Ile Tyr Leu Asn Trp Ile Glu Tyr Cys Ser Ser		
875	880	885
Arg Arg Ala Lys Pro Val Asp Val Asp Lys Asp Ser Ser Leu Val		
890	895	900
Thr Leu Cys Tyr Gly Leu Cys Val Leu Gly Arg Arg Ala Leu Gly		
905	910	915
Thr Ala Ser His His Met Ser Ser Asn Leu Glu Ser Phe Leu Tyr		
920	925	930
Gly Leu His Ala Leu Phe Lys Gly Asp Phe Arg Ile Ser Ser Ile		

Arg Asp Glu Trp	935	Phe Ala Asp Met	940	Glu Leu Leu Arg Lys Val	945
Val Val Pro Gly	950	Ile Arg Met Ser Ile	955	Leu His Gln Asp His	960
Phe Thr Ser Pro	965	Asp Glu Tyr Asp Asp	970	Pro Thr Val Leu Tyr Glu	975
Ala Ile Val Ser	980	His Glu Lys Asn Leu Val	985	Ile Ala His Glu Gly	990
Asp Pro Ala Trp	995	Arg Ser Ala Val Leu Ala	1000	Asn Ser Pro Ser Leu	1005
Leu Ala Leu Arg	1010	His Val Met Asp Asp	1015	Gly Thr Asn Glu Tyr Lys	1020
Ile Ile Met Leu	1025	Asn Arg Arg Tyr Leu Ser	1030	Phe Arg Val Ile Lys	1035
Val Asn Lys Glu	1040	Cys Val Arg Gly Leu Trp	1045	Ala Gly Gln Gln Gln	1050
Glu Leu Val Phe	1055	Leu Arg Asn Arg Asn Pro	1060	Glu Arg Gly Ser Ile	1065
Gln Asn Ala Lys	1070	Gln Ala Leu Arg Asn Met	1075	Ile Asn Ser Ser Cys	1080
Asp Gln Pro Ile	1085	Gly Tyr Pro Ile Phe Val	1090	Ser Pro Leu Thr Thr	1095
Ser Tyr Ser Asp	1100	Ser His Glu Gln Leu Lys	1105	Asp Ile Leu Gly Gly	1110
Pro Ile Ser Leu	1115	Gly Asn Ile Arg Asn Phe	1120	Ile Val Ser Thr Trp	1125
His Arg Leu Arg	1130	Lys Gly Cys Gly Ala Gly	1135	Cys Asn Ser Gly Gly	1140
Asn Ile Glu Asp	1145	Ser Asp Thr Gly Gly Gly	1150	Thr Ser Cys Thr Gly	1155
Asn Asn Ala Thr	1160	Thr Ala Asn Asn Pro His	1165	Ser Asn Val Thr Gln	1170
Gly Ser Ile Gly	1175	Asn Pro Gly Gln Gly Ser	1180	Gly Thr Gly Leu His	1185
Pro Pro Val Thr	1190	Ser Tyr Pro Pro Thr Leu	1195	Gly Thr Ser His Ser	1200
Ser His Ser Val	1205	Gln Ser Gly Leu Val Arg	1210	Gln Ser Pro Ala Arg	1215
Ala Ser Val Ala	1220	Ser Gln Ser Ser Tyr Cys	1225	Tyr Ser Ser Arg His	1230
Ser Ser Leu Arg	1235	Met Ser Thr Thr Gly Phe	1240	Val Pro Cys Arg Arg	1245
Ser Ser Thr Ser	1250	Gln Ile Ser Leu Arg Asn	1255	Leu Pro Ser Ser Ile	1260
Gln Ser Arg Leu	1265	Ser Met Val Asn Gln Met	1270	Glu Pro Ser Gly Gln	1275
Ser Gly Leu Ala	1280	Cys Val Gln His Gly Leu	1285	Pro Ser Ser Ser Ser	1290
Ser Ser Gln Ser	1295	Ile Pro Ala Cys Lys His	1300	His Thr Leu Val Gly	1305
Phe Leu Ala Thr	1310	Glu Gly Gly Gln Ser Ser	1315	Ala Thr Asp Ala Gln	1320
Pro Gly Asn Thr	1325	Leu Ser Pro Ala Asn Asn	1330	Ser His Ser Arg Lys	1335
Ala Glu Val Ile	1340	Tyr Arg Val Gln Ile Val	1345	Asp Pro Ser Gln Ile	1350
Leu Glu Gly Ile	1355	Asn Leu Ser Lys Arg Lys	1360	Glu Leu Gln Trp Pro	1365
Asp Glu Gly Ile	1370	Arg Leu Lys Ala Gly Arg	1375	Asn Ser Trp Lys Asp	1380
Trp Ser Pro Gln	1385	Glu Gly Met Glu Gly His	1390	Val Ile His Arg Trp	1395
	1400		1405		1410

Val Pro Cys Ser Arg Asp Pro Gly Thr Arg Ser His Ile Asp Lys  
 1415 1420 1425  
 Ala Val Leu Leu Val Gln Ile Asp Asp Lys Tyr Val Thr Val Ile  
 1430 1435 1440  
 Glu Thr Gly Val Leu Glu Leu Gly Ala Glu Val  
 1445 1450

<210> 23  
 <211> 184  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte ID No: 7494915CD1

<400> 23  
 Met Met Pro Gly Glu Lys Lys Gln Ser Gly Ser Gln Gln Gln Asn  
 1 5 10 15  
 Asn Gly Gln Ala Ser Lys Asn Arg Thr Gln Lys Glu Ile Val Thr  
 20 25 30  
 Gln Lys Arg Pro Ile Thr Ser Asn Glu Ile Glu Leu Val Val Lys  
 35 40 45  
 Lys Lys Leu Pro Arg Glu Lys Gly Pro Gly Pro Asp Gly Phe Ile  
 50 55 60  
 Ala Glu Phe Phe Arg Thr Val Lys Glu Glu Leu Glu Pro Thr Leu  
 65 70 75  
 Leu Lys Leu Phe Gln Lys Ile Glu Arg Glu Arg Ile Leu Pro Asn  
 80 85 90  
 Thr Phe Tyr Gly Val Ser Ile Thr Leu Met Pro Lys Pro Glu Lys  
 95 100 105  
 Asp Thr Thr Ala Thr Thr Thr Thr Thr Thr Asn Tyr Arg Pro  
 110 115 120  
 Thr Ser Leu Met Asn Val Asp Ser Lys Ile Leu Asn Lys Ile Leu  
 125 130 135  
 Ala Asn Gln Ile Gln Pro His Ile Lys Lys Ile Ile His His Asn  
 140 145 150  
 Gln Lys Leu Phe Ser Leu Ile Arg Ser His Leu Ser Ile Leu Ala  
 155 160 165  
 Phe Val Ala Ile Ala Phe Gly Val Leu Asp Val Lys Pro Leu Pro  
 170 175 180  
 Ile Pro Met His

<210> 24  
 <211> 407  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte ID No: 2073751CD1

<400> 24  
 Met Ala Ala Glu Ile Asp Phe Leu Arg Glu Gln Asn Arg Arg Leu  
 1 5 10 15  
 Asn Glu Asp Phe Arg Arg Tyr Gln Met Glu Ser Phe Ser Lys Tyr  
 20 25 30  
 Ser Ser Val Gln Lys Ala Val Cys Gln Gly Glu Gly Asp Asp Thr  
 35 40 45  
 Phe Glu Asn Leu Val Phe Asp Gln Ser Phe Leu Ala Pro Leu Val  
 50 55 60  
 Thr Glu Tyr Asp Lys His Leu Gly Glu Leu Asn Gly Gln Leu Lys

				65					70					75
Tyr	Tyr	Gln	Lys	Gln	Val	Gly	Glu	Met	Lys	Leu	Gln	Phe	Glu	Asn
				80					85					90
Val	Ile	Lys	Glu	Asn	Glu	Arg	Leu	His	Ser	Glu	Leu	Lys	Asp	Ala
				95					100					105
Val	Glu	Lys	Lys	Leu	Glu	Ala	Phe	Pro	Leu	Gly	Thr	Glu	Val	Gly
				110					115					120
Thr	Asp	Ile	Tyr	Ala	Asp	Asp	Glu	Thr	Val	Arg	Asn	Leu	Gln	Glu
				125					130					135
Gln	Leu	Gln	Leu	Ala	Asn	Gln	Glu	Lys	Thr	Gln	Ala	Val	Glu	Leu
				140					145					150
Trp	Gln	Thr	Val	Ser	Gln	Glu	Leu	Asp	Arg	Leu	His	Lys	Leu	Tyr
				155					160					165
Gln	Glu	His	Met	Thr	Glu	Ala	Gln	Ile	His	Val	Phe	Glu	Ser	Gln
				170					175					180
Lys	Gln	Lys	Asp	Gln	Leu	Phe	Asp	Phe	Gln	Gln	Leu	Thr	Lys	Gln
				185					190					195
Leu	His	Val	Thr	Asn	Glu	Asn	Met	Glu	Val	Thr	Asn	Gln	Gln	Phe
				200					205					210
Leu	Lys	Thr	Val	Thr	Glu	Gln	Ser	Val	Ile	Ile	Glu	Gln	Leu	Arg
				215					220					225
Lys	Lys	Leu	Arg	Gln	Ala	Lys	Leu	Glu	Leu	Arg	Val	Ala	Val	Ala
				230					235					240
Lys	Val	Glu	Glu	Leu	Thr	Asn	Val	Thr	Glu	Asp	Leu	Gln	Gly	Gln
				245					250					255
Met	Lys	Lys	Lys	Glu	Lys	Asp	Val	Val	Ser	Ala	His	Gly	Arg	Glu
				260					265					270
Glu	Ala	Ser	Asp	Arg	Arg	Leu	Gln	Gln	Leu	Gln	Ser	Ser	Ile	Lys
				275					280					285
Gln	Leu	Glu	Ile	Arg	Leu	Cys	Val	Thr	Ile	Gln	Glu	Ala	Asn	Gln
				290					295					300
Leu	Arg	Thr	Glu	Asn	Thr	His	Leu	Glu	Lys	Gln	Thr	Arg	Glu	Leu
				305					310					315
Gln	Ala	Lys	Cys	Asn	Glu	Leu	Glu	Asn	Glu	Arg	Tyr	Glu	Ala	Ile
				320					325					330
Val	Arg	Ala	Arg	Asn	Ser	Met	Gln	Leu	Leu	Glu	Glu	Ala	Asn	Leu
				335					340					345
Gln	Lys	Ser	Gln	Ala	Leu	Leu	Glu	Glu	Lys	Gln	Lys	Glu	Glu	Asp
				350					355					360
Ile	Glu	Lys	Met	Lys	Glu	Thr	Val	Ser	Arg	Phe	Val	Gln	Asp	Ala
				365					370					375
Thr	Ile	Arg	Thr	Lys	Lys	Glu	Val	Ala	Asn	Thr	Lys	Lys	Gln	Cys
				380					385					390
Asn	Ile	Gln	Ile	Ser	Arg	Leu	Thr	Glu	Glu	Leu	Ser	Ala	Leu	Gln
				395					400					405

Met Glu

<210> 25  
 <211> 261  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte ID No: 3178841CD1

<400> 25  
 Met Thr Cys Leu Ala Pro Thr Met Ser Ala Glu Leu Asn Val Pro  
 1 5 10 15  
 Ile Asp Pro Ser Ala Pro Ala Cys Pro Glu Pro Gly His Lys Gly  
 20 25 30  
 Met Asp Tyr Arg Asp Trp Val Arg Arg Ser Tyr Leu Glu Leu Val



	35		40		45
Thr Ser Asn His	His Ser Val Gln Ala Leu Ser Trp Arg Lys Leu				
	50		55		60
Tyr Leu Ser Arg	Ala Lys Leu Lys Ala Ser Ser Arg Thr Ser Ala				
	65		70		75
Leu Leu Ser Gly	Phe Ala Met Val Ala Met Val Glu Val Gln Leu				
	80		85		90
Glu Thr Gln Tyr	Gln Tyr Pro Arg Pro Leu Leu Ile Ala Phe Ser				
	95		100		105
Ala Cys Thr Thr	Val Leu Val Ala Val His Leu Phe Ala Leu Leu				
	110		115		120
Ile Ser Thr Cys	Ile Leu Pro Asn Val Glu Ala Val Ser Asn Ile				
	125		130		135
His Asn Leu Asn	Ser Ile Ser Glu Ser Pro His Glu Arg Met His				
	140		145		150
Pro Tyr Ile Glu	Leu Ala Trp Gly Phe Ser Thr Val Leu Gly Ile				
	155		160		165
Leu Leu Phe Leu	Ala Glu Val Val Leu Leu Cys Trp Ile Lys Phe				
	170		175		180
Leu Pro Val Asp	Ala Arg Arg Gln Pro Gly Pro Pro Pro Gly Pro				
	185		190		195
Gly Ser His Thr	Gly Trp Gln Ala Ala Leu Val Ser Thr Ile Ile				
	200		205		210
Met Val Pro Val	Gly Leu Ile Phe Val Val Phe Thr Ile His Phe				
	215		220		225
Tyr Arg Ser Leu	Val Arg His Lys Thr Glu Arg His Asn Arg Glu				
	230		235		240
Ile Glu Glu Leu	His Lys Leu Lys Val Gln Leu Asp Gly His Glu				
	245		250		255
Arg Ser Leu Gln	Val Leu				
	260				

&lt;210&gt; 26

&lt;211&gt; 209

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte ID No: 3674807CD1

&lt;400&gt; 26

Met Ala Thr Ile	Ala Ala Ala Phe Glu Ala Leu Met Asp Gly				
1	5		10		15
Val Thr Cys Trp	Asp Val Pro Arg Gly Pro Ile Pro Ser Glu Leu				
	20		25		30
Leu Leu Ile Gly	Glu Ala Ala Phe Pro Val Met Val Asn Asp Lys				
	35		40		45
Gly Gln Val Leu	Ile Ala Ala Ser Ser Tyr Gly Arg Gly Arg Leu				
	50		55		60
Val Val Val Ser	His Glu Gly Tyr Leu Ser His Ala Gly Leu Ala				
	65		70		75
Pro Phe Leu Leu	Asn Ala Val Ser Trp Leu Cys Pro Cys Pro Gly				
	80		85		90
Ala Pro Val Gly	Val His Pro Ser Leu Ala Pro Leu Val Asn Ile				
	95		100		105
Leu Gln Asp Ala	Gly Leu Glu Ala Gln Val Lys Pro Glu Pro Gly				
	110		115		120
Glu Pro Leu Gly	Val Tyr Cys Ile Asn Ala Tyr Asn Asp Thr Leu				
	125		130		135
Thr Ala Thr Leu	Ile Gln Phe Val Lys His Gly Gly Gly Leu Leu				
	140		145		150
Ile Gly Gly Gln	Ala Trp Tyr Trp Ala Ser Gln His Gly Pro Asp				

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<210> 27
<211> 333
<212> PRT
<213> Homo sapiens
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<220>  
<221> misc_feature  
<223> Incyte ID No: 1794922CD1
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<210> 28  
 <211> 257  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte ID No: 1795509CD1

<400> 28

Met	Val	Ala	Glu	Lys	Glu	Thr	Leu	Ser	Leu	Asn	Lys	Cys	Pro	Asp	
1				5					10					15	
Lys	Met	Pro	Lys	Arg	Thr	Lys	Leu	Leu	Ala	Gln	Gln	Pro	Leu	Pro	
				20					25					30	
Val	His	Gln	Pro	His	Ser	Leu	Val	Ser	Glu	Gly	Phe	Thr	Val	Lys	
				35					40					45	
Ala	Met	Met	Lys	Asn	Ser	Val	Val	Arg	Gly	Pro	Pro	Ala	Ala	Gly	
				50					55					60	
Ala	Phe	Lys	Glu	Arg	Pro	Thr	Lys	Pro	Thr	Ala	Phe	Arg	Lys	Phe	
				65					70					75	
Tyr	Glu	Arg	Gly	Asp	Phe	Pro	Ile	Ala	Leu	Glu	His	Asp	Ser	Lys	
				80					85					90	
Gly	Asn	Lys	Ile	Ala	Trp	Lys	Val	Glu	Ile	Glu	Lys	Leu	Asp	Tyr	
				95					100					105	
His	His	Tyr	Leu	Pro	Leu	Phe	Phe	Asp	Gly	Leu	Cys	Glu	Met	Thr	
				110					115					120	
Phe	Pro	Tyr	Glu	Phe	Phe	Ala	Arg	Gln	Gly	Ile	His	Asp	Met	Leu	
				125					130					135	
Glu	His	Gly	Gly	Asn	Lys	Ile	Leu	Pro	Val	Leu	Pro	Gln	Leu	Ile	
				140					145					150	
Ile	Pro	Ile	Lys	Asn	Ala	Leu	Asn	Leu	Arg	Asn	Arg	Gln	Val	Ile	
				155					160					165	
Cys	Val	Thr	Leu	Lys	Val	Leu	Gln	His	Leu	Val	Val	Ser	Ala	Glu	
				170					175					180	
Met	Val	Gly	Lys	Ala	Leu	Val	Pro	Tyr	Tyr	Arg	Gln	Ile	Leu	Pro	
				185					190					195	
Val	Leu	Asn	Ile	Phe	Lys	Asn	Met	Asn	Val	Asn	Ser	Gly	Asp	Gly	
				200					205					210	
Ile	Asp	Tyr	Ser	Gln	Gln	Lys	Arg	Glu	Asn	Ile	Gly	Asp	Leu	Ile	
				215					220					225	
Gln	Glu	Thr	Leu	Glu	Ala	Phe	Glu	Arg	Tyr	Gly	Gly	Glu	Asn	Ala	
				230					235					240	
Phe	Ile	Asn	Ile	Lys	Tyr	Val	Val	Pro	Thr	Tyr	Glu	Ser	Cys	Leu	
				245					250					255	

Leu Asn

<210> 29  
 <211> 293  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte ID No: 2017180CD1

<400> 29

Met	Arg	Val	Asp	Ser	Ser	Ala	Asp	Pro	Thr	Met	Ser	Gln	Glu	Gln	
1				5					10					15	
Gly	Pro	Gly	Ser	Ser	Thr	Pro	Pro	Ser	Ser	Pro	Thr	Leu	Leu	Asp	
				20					25					30	

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Ala Leu Leu Gln Asn Leu Tyr Asp Phe Gly Gly Thr Glu Gly Glu
      35      40      45
Thr Glu Gln Lys Lys Ile Ile Lys Lys Arg Glu Asn Lys Lys Arg
      50      55      60
Asp Val Met Ala Ser Ala Ala Leu Ala Glu Pro Ser Pro Leu
      65      70      75
Pro Gly Ser Leu Ile Arg Gly Gln Arg Lys Ser Ala Ser Ser Phe
      80      85      90
Phe Lys Glu Leu Arg Glu Glu Arg His Cys Ala Pro Ser Gly Thr
      95     100     105
Pro Thr Gly Pro Glu Ile Leu Ala Ala Val Pro Pro Ser Ser
     110     115     120
Leu Lys Asn Asn Arg Glu Gln Val Glu Val Val Glu Phe His Ser
     125     130     135
Asn Lys Lys Arg Lys Leu Thr Pro Asp His Asn Lys Asn Thr Lys
     140     145     150
Gln Ala Asn Pro Ser Val Leu Glu Arg Asp Val Asp Thr Gln Glu
     155     160     165
Phe Asn Leu Glu Lys Ala Arg Leu Glu Val His Arg Phe Gly Ile
     170     175     180
Thr Gly Tyr Gly Lys Gly Lys Glu Arg Ile Leu Glu Gln Glu Arg
     185     190     195
Ala Ile Met Leu Gly Ala Lys Pro Pro Lys Lys Ser Tyr Val Asn
     200     205     210
Tyr Lys Val Leu Gln Glu Gln Ile Lys Glu Lys Lys Ala Ala Lys
     215     220     225
Glu Glu Glu Lys Arg Leu Ala Gln Glu Thr Asp Ile Phe Lys Lys
     230     235     240
Lys Lys Arg Lys Gly Gln Glu Asp Arg Lys Ser Lys Lys Lys Ser
     245     250     255
Ala Pro Ser Ile Leu Ser Asn Gly Arg Ile Gly Gln Val Gly Lys
     260     265     270
Phe Lys Asn Gly Thr Leu Ile Leu Ser Pro Val Asp Ile Lys Lys
     275     280     285
Ile Asn Ser Ser Arg Val Ala Lys
     290

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&lt;210&gt; 30

&lt;211&gt; 598

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte ID No: 219442CD1

&lt;400&gt; 30

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Met Ala Ala Ser Val Thr Asn Ala Val Pro Pro His Asn Phe Lys
  1      5      10      15
Ser Gln Glu Val Thr Pro Ala Cys Leu Asp Gly Lys Ser Leu Arg
     20      25      30
Ala Gly Ile Thr Glu Val Lys Glu Pro Ser Val Thr Ser Pro Thr
     35      40      45
Pro Ser Asp Ile Gln Gln Asn Lys Gly Leu Pro Lys Pro Glu Phe
     50      55      60
Arg Phe Lys Gly Gln Ser Thr Lys Ser Asp Ser Ala Glu Asp Tyr
     65      70      75
Leu Leu Trp Lys Arg Leu Gln Gly Val Ser Ala Ala Cys Pro Ala
     80      85      90
Pro Ser Ser Ala Ala His Gln Leu Glu His Leu Ser Ala Lys Leu
     95     100     105
Gln Lys Ile Asp Glu Gln Leu Leu Ala Ile Gln Asn Ile Ala Glu
    110     115     120

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Asn	Ile	Glu	Gln	Asp	Phe	Pro	Lys	Pro	Glu	Met	Leu	Asp	Leu	His
				125					130					135
Cys	Asp	Lys	Ile	Gly	Pro	Val	Asp	His	Ile	Glu	Phe	Ser	Ser	Gly
				140					145					150
Pro	Glu	Phe	Lys	Lys	Thr	Leu	Ala	Ser	Lys	Thr	Ile	Ser	Ile	Ser
				155					160					165
Glu	Glu	Val	Arg	Phe	Leu	Thr	His	Met	Asp	Glu	Glu	Asp	Gln	Ser
				170					175					180
Asp	Lys	Lys	Glu	Thr	Ser	Glu	Pro	Glu	Phe	Ser	Ile	Thr	Glu	Asn
				185					190					195
Tyr	Ser	Gly	Gln	Lys	Thr	Cys	Val	Phe	Pro	Thr	Ala	Asp	Ser	Ala
				200					205					210
Val	Ser	Leu	Ser	Ser	Ser	Ser	Asp	Gln	Asn	Thr	Thr	Ser	Pro	Gly
				215					220					225
Met	Asn	Ser	Ser	Asp	Glu	Leu	Cys	Glu	Ser	Val	Ser	Val	His	Pro
				230					235					240
Leu	Gln	Met	Thr	Gly	Leu	Thr	Asp	Ile	Ala	Asp	Ile	Ile	Asp	Asp
				245					250					255
Leu	Ile	Ile	Lys	Asp	Gly	Val	Ser	Ser	Glu	Glu	Leu	Gly	Leu	Thr
				260					265					270
Glu	Gln	Ala	Met	Gly	Thr	Ser	Arg	Ile	Gln	His	Tyr	Ser	Gly	Arg
				275					280					285
His	Ser	Gln	Arg	Thr	Asp	Lys	Glu	Arg	Arg	Glu	Ile	Gln	Ala	Trp
				290					295					300
Met	Lys	Arg	Lys	Arg	Lys	Glu	Arg	Met	Ala	Lys	Tyr	Leu	Asn	Glu
				305					310					315
Leu	Ala	Glu	Lys	Arg	Gly	Gln	Glu	His	Asp	Pro	Phe	Cys	Pro	Arg
				320					325					330
Ser	Asn	Pro	Leu	Tyr	Met	Thr	Ser	Arg	Glu	Ile	Arg	Leu	Arg	Gln
				335					340					345
Lys	Met	Lys	His	Glu	Lys	Asp	Arg	Leu	Leu	Leu	Ser	Glu	His	Tyr
				350					355					360
Ser	Arg	Arg	Ile	Ser	Gln	Ala	Tyr	Gly	Leu	Met	Asn	Glu	Leu	Leu
				365					370					375
Ser	Glu	Ser	Val	Gln	Leu	Pro	Thr	Leu	Pro	Gln	Lys	Pro	Leu	Pro
				380					385					390
Asn	Lys	Pro	Ser	Pro	Thr	Gln	Ser	Ser	Ser	Cys	Gln	His	Cys	Pro
				395					400					405
Ser	Pro	Arg	Gly	Glu	Asn	Gln	His	Gly	His	Ser	Phe	Leu	Ile	Asn
				410					415					420
Arg	Pro	Gly	Lys	Val	Lys	Tyr	Met	Ser	Lys	Pro	Ser	Tyr	Ile	His
				425					430					435
Lys	Arg	Lys	Ser	Phe	Gly	Gln	Pro	Gln	Gly	Ser	Pro	Trp	Pro	His
				440					445					450
Gly	Thr	Ala	Thr	Phe	Thr	Ile	Gln	Lys	Lys	Ala	Gly	Gly	Ala	Lys
				455					460					465
Ala	Ala	Val	Arg	Lys	Ala	Thr	Gln	Ser	Pro	Val	Thr	Phe	Gln	Lys
				470					475					480
Gly	Ser	Asn	Ala	Pro	Cys	His	Ser	Leu	Gln	His	Thr	Lys	Lys	His
				485					490					495
Gly	Ser	Ala	Gly	Leu	Ala	Pro	Gln	Thr	Lys	Gln	Val	Cys	Val	Glu
				500					505					510
Tyr	Glu	Arg	Glu	Glu	Thr	Val	Val	Ser	Pro	Trp	Thr	Ile	Pro	Ser
				515					520					525
Glu	Ile	His	Lys	Ile	Leu	His	Glu	Ser	His	Asn	Ser	Leu	Leu	Gln
				530					535					540
Asp	Leu	Ser	Pro	Thr	Glu	Glu	Glu	Glu	Pro	Glu	His	Pro	Phe	Gly
				545					550					555
Val	Gly	Gly	Val	Asp	Ser	Val	Ser	Glu	Ser	Thr	Gly	Ser	Ile	Leu
				560					565					570
Ser	Lys	Leu	Asp	Trp	Asn	Ala	Ile	Glu	Asp	Met	Val	Ala	Ser	Val
				575					580					585
Glu	Asp	Gln	Gly	Leu	Ser	Val	His	Trp	Ala	Leu	Asp	Leu		

590

595

<210> 31  
 <211> 470  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte ID No: 2597459CD1

&lt;400&gt; 31

Met	Pro	Ser	Glu	Arg	Cys	Leu	Ser	Ile	Gln	Glu	Met	Leu	Thr	Gly
1				5					10					15
Gln	Arg	Leu	Cys	His	Ser	Glu	Ser	His	Asn	Asp	Ser	Val	Leu	Ala
				20					25					30
Ala	Leu	Asn	Gln	Gln	Arg	Ser	Asp	Gly	Ile	Leu	Cys	Asp	Ile	Thr
				35					40					45
Leu	Ile	Ala	Glu	Glu	Gln	Lys	Phe	His	Ala	His	Lys	Ala	Val	Leu
				50					55					60
Ala	Ala	Cys	Ser	Asp	Tyr	Phe	Arg	Ala	Met	Phe	Ser	Leu	Cys	Met
				65					70					75
Val	Glu	Ser	Gly	Ala	Asp	Glu	Val	Asn	Leu	His	Gly	Val	Thr	Ser
				80					85					90
Leu	Gly	Leu	Lys	Gln	Ala	Leu	Glu	Phe	Ala	Tyr	Thr	Gly	Gln	Ile
				95					100					105
Leu	Leu	Glu	Pro	Gly	Val	Ile	Gln	Asp	Val	Leu	Ala	Ala	Gly	Ser
				110					115					120
His	Leu	Gln	Leu	Leu	Glu	Leu	Leu	Asn	Leu	Cys	Ser	His	Tyr	Leu
				125					130					135
Ile	Gln	Glu	Leu	Asn	Ser	Phe	Asn	Tyr	Leu	Asp	Leu	Tyr	Arg	Leu
				140					145					150
Ala	Asp	Leu	Phe	Asn	Leu	Thr	Leu	Leu	Glu	Lys	Ala	Val	Ile	Asp
				155					160					165
Phe	Leu	Val	Lys	His	Leu	Ser	Glu	Leu	Leu	Lys	Ser	Arg	Pro	Glu
				170					175					180
Glu	Val	Leu	Thr	Leu	Pro	Tyr	Cys	Leu	Leu	Gln	Glu	Val	Leu	Lys
				185					190					195
Ser	Asp	Arg	Leu	Thr	Ser	Leu	Ser	Glu	Glu	Gln	Ile	Trp	Gln	Leu
				200					205					210
Ala	Val	Arg	Trp	Leu	Glu	His	Asn	Cys	His	Tyr	Gln	Tyr	Met	Asp
				215					220					225
Glu	Leu	Leu	Gln	Tyr	Ile	Arg	Phe	Gly	Leu	Met	Asp	Val	Asp	Thr
				230					235					240
Leu	His	Thr	Val	Ala	Leu	Ser	His	Pro	Leu	Val	Gln	Ala	Ser	Glu
				245					250					255
Thr	Ala	Thr	Ala	Leu	Val	Asn	Glu	Ala	Leu	Glu	Tyr	His	Gln	Ser
				260					265					270
Ile	Tyr	Ala	Gln	Pro	Val	Trp	Gln	Thr	Arg	Arg	Thr	Lys	Pro	Arg
				275					280					285
Phe	Gln	Ser	Asp	Thr	Leu	Tyr	Ile	Ile	Gly	Gly	Lys	Lys	Arg	Glu
				290					295					300
Val	Cys	Lys	Val	Lys	Glu	Leu	Arg	Tyr	Phe	Asn	Pro	Val	Asp	Gln
				305					310					315
Glu	Asn	Ala	Leu	Ile	Ala	Ala	Ile	Ala	Asn	Trp	Ser	Glu	Leu	Ala
				320					325					330
Pro	Met	Pro	Val	Gly	Arg	Ser	His	His	Cys	Val	Ala	Val	Met	Gly
				335					340					345
Asp	Phe	Leu	Phe	Val	Ala	Gly	Gly	Glu	Val	Glu	His	Ala	Ser	Gly
				350					355					360
Arg	Thr	Cys	Ala	Val	Arg	Thr	Ala	Cys	Arg	Tyr	Asp	Pro	Arg	Ser
				365					370					375
Asn	Ser	Trp	Ala	Glu	Ile	Ala	Pro	Met	Lys	Asn	Cys	Arg	Glu	His

Phe Val Leu Gly	380	385	390
Ala Met Glu Glu Tyr		Leu Tyr Ala Val Gly Gly	
	395	400	405
Arg Asn Glu Leu Arg		Thr Val Glu Arg Tyr Cys	
	410	415	420
Pro Lys Lys Asn Lys		Trp Thr Phe Val Gln Ser Phe Asp Arg Ser	
	425	430	435
Leu Ser Cys His Ala		Gly Tyr Val Ala Asp Gly Leu Leu Trp Ile	
	440	445	450
Ser Gly Arg Thr Tyr		Leu Met Leu Asp Leu Ser Lys His Thr Phe	
	455	460	465
Ile Val Val Tyr Ile			
	470		

&lt;210&gt; 32

&lt;211&gt; 311

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte ID No: 2783863CD1

&lt;400&gt; 32

Met His Gln Lys Leu	Leu Lys Ser Ala	His Tyr Ile Glu Leu Gly
1	5	10
Ser Tyr Gln Tyr Trp	Pro Val Leu Val Pro	Arg Gly Ile Arg Leu
	20	25
Tyr Thr Tyr Glu Gln	Ile Pro Gly Ser Leu	Lys Asp Asn Pro Tyr
	35	40
Ile Thr Asp Gly Tyr	Arg Ala Tyr Leu Pro	Ser Arg Leu Cys Ile
	50	55
Lys Ser Leu Phe Ile	Leu Ser Asn Glu Thr	Val Asn Ile Trp Ser
	65	70
His Leu Leu Gly Phe	Phe Leu Phe Phe Thr	Leu Gly Ile Tyr Asp
	80	85
Met Thr Ser Val Leu	Pro Ser Ala Ser Ala	Ser Arg Glu Asp Phe
	95	100
Val Ile Cys Ser Ile	Cys Leu Phe Cys Phe	Gln Val Cys Met Leu
	110	115
Cys Ser Val Gly Tyr	His Leu Phe Ser Cys	His Arg Ser Glu Lys
	125	130
Thr Cys Arg Arg Trp	Met Ala Leu Asp Tyr	Ala Gly Ile Ser Ile
	140	145
Gly Ile Leu Gly Cys	Tyr Val Ser Gly Val	Phe Tyr Ala Phe Tyr
	155	160
Cys Asn Asn Tyr Trp	Arg Gln Val Tyr Leu	Ile Thr Val Leu Ala
	170	175
Met Ile Leu Ala Val	Phe Phe Ala Gln Ile	His Pro Asn Tyr Leu
	185	190
Thr Gln Gln Trp Gln	Arg Leu Arg Ser Ile	Ile Phe Cys Ser Val
	200	205
Ser Gly Tyr Gly Val	Ile Pro Thr Leu His	Trp Val Trp Leu Asn
	215	220
Gly Gly Ile Gly Ala	Pro Ile Val Gln Asp	Phe Ala Pro Arg Val
	230	235
Ile Val Met Tyr Met	Ile Ala Leu Leu Ala	Phe Leu Phe Tyr Ile
	245	250
Ser Lys Val Pro Glu	Arg Tyr Phe Pro Gly	Gln Leu Asn Tyr Leu
	260	265
Gly Ser Ser His Gln	Ile Trp His Ile Leu	Ala Val Val Met Leu
	275	280
Tyr Trp Trp His Gln	Ser Thr Val Tyr Val	Met Gln Tyr Arg His

Ser Lys Pro Cys Pro Asp Tyr Val Ser His Leu  
 290 295 300  
 305 310

<210> 33  
 <211> 894  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte ID No: 2902971CD1

<400> 33  
 Met Ala Thr Ser Met Ala Ala Ala Ser Gly Arg Phe Glu Ser Ala  
 1 5 10 15  
 Lys Ser Ile Glu Glu Arg Lys Glu Gln Thr Arg Asn Ala Arg Ala  
 20 25 30  
 Glu Val Leu Arg Gln Ala Lys Ala Asn Phe Glu Lys Glu Glu Arg  
 35 40 45  
 Arg Lys Glu Leu Lys Arg Leu Arg Gly Glu Asp Thr Trp Met Leu  
 50 55 60  
 Pro Asp Val Asn Glu Arg Ile Glu Gln Phe Ser Gln Glu His Ser  
 65 70 75  
 Val Lys Lys Lys Lys Lys Lys Asp Lys His Ser Lys Lys Ala Lys  
 80 85 90  
 Lys Glu Lys Lys Lys Lys Ser Lys Lys Gln Lys Tyr Glu Lys Asn  
 95 100 105  
 Asn Glu Ser Ser Asp Ser Ser Ser Ser Glu Asp Glu Trp Val  
 110 115 120  
 Glu Ala Val Pro Ser Gln Thr Pro Asp Lys Glu Lys Ala Trp Lys  
 125 130 135  
 Val Lys Asp Glu Lys Ser Gly Lys Asp Asp Thr Gln Ile Ile Lys  
 140 145 150  
 Arg Asp Glu Trp Met Thr Val Asp Phe Met Ser Val Lys Thr Val  
 155 160 165  
 Ser Ser Ser Ser Leu Lys Ala Glu Lys Glu Thr Met Arg Lys Ile  
 170 175 180  
 Glu Gln Glu Lys Asn Gln Ala Leu Glu Gln Ser Lys Leu Met Glu  
 185 190 195  
 Arg Glu Leu Asn Pro Tyr Trp Lys Asp Gly Thr Gly Leu Pro  
 200 205 210  
 Pro Glu Asp Cys Ser Val Ser Ser Ile Thr Lys Val Ser Val Val  
 215 220 225  
 Glu Asp Gly Gly Leu Ser Trp Leu Arg Lys Ser Tyr Leu Arg Met  
 230 235 240  
 Lys Glu Gln Ala Glu Lys Gln Ser Arg Asn Phe Glu Asp Ile Val  
 245 250 255  
 Ala Glu Arg Tyr Gly Ser Met Glu Ile Phe Gln Ser Lys Leu Glu  
 260 265 270  
 Asp Ala Glu Lys Ala Ala Ser Thr Lys Glu Asp Tyr Arg Arg Glu  
 275 280 285  
 Arg Trp Arg Lys Pro Thr Tyr Ser Asp Lys Ala Gln Asn Cys Gln  
 290 295 300  
 Glu Ser Arg Glu Ser Asp Leu Val Lys Tyr Gly Asn Ser Ser Arg  
 305 310 315  
 Asp Arg Tyr Ala Thr Thr Asp Thr Ala Lys Asn Ser Asn Asn Glu  
 320 325 330  
 Lys Phe Ile Gly Asp Glu Lys Asp Lys Arg Pro Gly Ser Leu Glu  
 335 340 345  
 Thr Cys Arg Arg Glu Ser Asn Pro Arg Gln Asn Gln Glu Phe Ser  
 350 355 360  
 Phe Gly Asn Leu Arg Ala Lys Phe Leu Arg Pro Ser Asp Asp Glu



	365		370		375
Glu Leu Ser Phe	His Ser Lys Gly Arg	Lys Phe Glu Pro Leu Ser			
	380		385		390
Ser Ser Ser Ala	Leu Val Ala Gln Gly	Ser Leu Cys Ser Gly Phe			
	395		400		405
Arg Lys Pro Thr	Lys Asn Ser Glu Glu	Arg Leu Thr Ser Trp Ser			
	410		415		420
Arg Ser Asp Gly	Arg Gly Asp Lys Lys	His Ser Asn Gln Lys Pro			
	425		430		435
Ser Glu Thr Ser	Thr Asp Glu Tyr Gln	His Val Pro Glu Asp Pro			
	440		445		450
Arg Glu Lys Ser	Gln Asp Glu Val Leu	Arg Asp Asp Pro Pro Lys			
	455		460		465
Lys Glu His Leu	Arg Asp Thr Lys Ser	Thr Phe Ala Gly Ser Pro			
	470		475		480
Glu Arg Glu Ser	Ile His Ile Leu Ser	Val Asp Glu Lys Asn Lys			
	485		490		495
Leu Gly Ala Lys	Ile Ile Lys Ala Glu	Met Met Gly Asn Met Glu			
	500		505		510
Leu Ala Glu Gln	Leu Lys Val Gln Leu	Glu Lys Ala Asn Lys Phe			
	515		520		525
Lys Glu Thr Ile	Thr Gln Ile Pro Lys	Lys Ser Gly Val Glu Asn			
	530		535		540
Glu Asp Gln Gln	Glu Val Ile Leu Val	Arg Thr Asp Gln Ser Gly			
	545		550		555
Arg Val Trp Pro	Val Asn Thr Pro Gly	Lys Ser Leu Glu Ser Gln			
	560		565		570
Gly Gly Arg Arg	Lys Arg Gln Met Val	Ser Thr His Glu Glu Arg			
	575		580		585
Glu Arg Val Arg	Tyr Phe His Asp Asp	Asp Asn Leu Ser Leu Asn			
	590		595		600
Asp Leu Val Lys	Asn Glu Lys Met Gly	Thr Ala Glu Asn Gln Asn			
	605		610		615
Lys Leu Phe Met	Arg Met Ala Ser Lys	Phe Met Gly Lys Thr Asp			
	620		625		630
Gly Asp Tyr Tyr	Thr Leu Asp Asp Met	Phe Val Ser Lys Ala Ala			
	635		640		645
Glu Arg Glu Arg	Leu Gly Glu Glu Glu	Glu Asn Gln Arg Lys Lys			
	650		655		660
Ala Ile Ala Glu	His Arg Ser Leu Ala	Ala Gln Met Glu Lys Cys			
	665		670		675
Leu Tyr Cys Phe	Asp Ser Ser Gln Phe	Pro Lys His Leu Ile Val			
	680		685		690
Ala Ile Gly Val	Lys Val Tyr Leu Cys	Leu Pro Asn Val Arg Ser			
	695		700		705
Leu Thr Glu Gly	His Cys Leu Ile Val	Pro Leu Gln His His Arg			
	710		715		720
Ala Ala Thr Leu	Leu Asp Glu Asp Ile	Trp Glu Glu Ile Gln Met			
	725		730		735
Phe Arg Lys Ser	Leu Val Lys Met Phe	Glu Asp Lys Gly Leu Asp			
	740		745		750
Cys Ile Phe Leu	Glu Thr Asn Met Ser	Met Lys Lys Gln Tyr His			
	755		760		765
Met Val Tyr Glu	Cys Ile Pro Leu Pro	Lys Glu Val Gly Asp Met			
	770		775		780
Ala Pro Ile Tyr	Phe Lys Lys Ala Ile	Met Glu Ser Asp Glu Glu			
	785		790		795
Trp Ser Met Asn	Lys Lys Leu Met Asp	Leu Ser Ser Lys Asp Ile			
	800		805		810
Arg Lys Ser Val	Pro Arg Gly Leu Pro	Tyr Phe Ser Val Asp Phe			
	815		820		825
Gly Leu His Gly	Gly Phe Ala His Val	Ile Glu Asp Gln His Lys			
	830		835		840

Phe	Pro	His	Tyr	Phe	Gly	Lys	Glu	Ile	Ile	Gly	Gly	Met	Leu	Asp	
				845					850					855	
Ile	Glu	Pro	Arg	Leu	Trp	Arg	Lys	Gly	Ile	Arg	Glu	Ser	Phe	Glu	
				860					865					870	
Asp	Gln	Arg	Lys	Lys	Ala	Leu	Gln	Phe	Ala	Gln	Trp	Trp	Lys	Pro	
				875					880					885	
Tyr	Asp	Phe	Thr	Lys	Ser	Lys	Asn	Tyr							
				890											

&lt;210&gt; 34

&lt;211&gt; 653

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte ID No: 368660CD1

&lt;400&gt; 34

Met	Asp	Arg	Asp	Leu	Leu	Arg	Gln	Ser	Leu	Asn	Cys	His	Gly	Ser	
1				5					10					15	
Ser	Leu	Leu	Ser	Leu	Leu	Arg	Ser	Glu	Gln	Gln	Asp	Asn	Pro	His	
				20					25					30	
Phe	Arg	Ser	Leu	Leu	Gly	Ser	Ala	Ala	Glu	Pro	Ala	Arg	Gly	Pro	
				35					40					45	
Pro	Pro	Gln	His	Pro	Leu	Gln	Gly	Arg	Lys	Glu	Lys	Arg	Val	Asp	
				50					55					60	
Asn	Ile	Glu	Ile	Gln	Lys	Phe	Ile	Ser	Lys	Lys	Ala	Asp	Leu	Leu	
				65					70					75	
Phe	Ala	Leu	Ser	Trp	Lys	Ser	Asp	Ala	Pro	Ala	Thr	Ser	Glu	Ile	
				80					85					90	
Asn	Glu	Asp	Ser	Glu	Asp	His	Tyr	Ala	Ile	Met	Pro	Pro	Leu	Glu	
				95					100					105	
Gln	Phe	Met	Glu	Ile	Pro	Ser	Met	Asp	Arg	Arg	Glu	Leu	Phe	Phe	
				110					115					120	
Arg	Asp	Ile	Glu	Arg	Gly	Asp	Ile	Val	Ile	Gly	Arg	Ile	Ser	Ser	
				125					130					135	
Ile	Arg	Glu	Phe	Gly	Phe	Phe	Met	Val	Leu	Ile	Cys	Leu	Gly	Ser	
				140					145					150	
Gly	Ile	Met	Arg	Asp	Ile	Ala	His	Leu	Glu	Ile	Thr	Ala	Leu	Cys	
				155					160					165	
Pro	Leu	Arg	Asp	Val	Pro	Ser	His	Ser	Asn	His	Gly	Asp	Pro	Leu	
				170					175					180	
Ser	Tyr	Tyr	Gln	Thr	Gly	Asp	Ile	Ile	Arg	Ala	Gly	Ile	Lys	Asp	
				185					190					195	
Ile	Asp	Arg	Tyr	His	Glu	Lys	Leu	Ala	Val	Ser	Leu	Tyr	Ser	Ser	
				200					205					210	
Ser	Leu	Pro	Pro	His	Leu	Ser	Gly	Ile	Lys	Leu	Gly	Val	Ile	Ser	
				215					220					225	
Ser	Glu	Glu	Leu	Pro	Leu	Tyr	Tyr	Arg	Arg	Ser	Val	Glu	Leu	Asn	
				230					235					240	
Ser	Asn	Ser	Leu	Glu	Ser	Tyr	Glu	Asn	Val	Met	Gln	Ser	Ser	Leu	
				245					250					255	
Gly	Phe	Val	Asn	Pro	Gly	Val	Val	Glu	Phe	Leu	Leu	Glu	Lys	Leu	
				260					265					270	
Gly	Ile	Asp	Glu	Ser	Asn	Pro	Pro	Ser	Leu	Met	Arg	Gly	Leu	Gln	
				275					280					285	
Ser	Lys	Asn	Phe	Ser	Glu	Asp	Asp	Phe	Ala	Ser	Ala	Leu	Arg	Lys	
				290					295					300	
Lys	Gln	Ser	Ala	Ser	Trp	Ala	Leu	Lys	Cys	Val	Lys	Ile	Gly	Val	
				305					310					315	
Asp	Tyr	Phe	Lys	Val	Gly	Arg	His	Val	Asp	Ala	Met	Asn	Glu	Tyr	
				320					325					330	

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Asn Lys Ala Leu Glu Ile Asp Lys Gln Asn Val Glu Ala Leu Val
335 340 345
Ala Arg Gly Ala Leu Tyr Ala Thr Lys Gly Ser Leu Asn Lys Ala
350 355 360
Ile Glu Asp Phe Glu Leu Ala Leu Glu Asn Cys Pro Thr His Arg
365 370 375
Asn Ala Arg Lys Tyr Leu Cys Gln Thr Leu Val Glu Arg Gly Gly
380 385 390
Gln Leu Glu Glu Glu Glu Lys Phe Leu Asn Ala Glu Ser Tyr Tyr
395 400 405
Lys Lys Ala Leu Ala Leu Asp Glu Thr Phe Lys Asp Ala Glu Asp
410 415 420
Ala Leu Gln Lys Leu His Lys Tyr Met Gln Lys Ser Leu Glu Leu
425 430 435
Arg Glu Lys Gln Ala Glu Lys Glu Glu Lys Gln Lys Thr Lys Lys
440 445 450
Ile Glu Thr Ser Ala Glu Lys Leu Arg Asn Val Leu Lys Glu Glu
455 460 465
Lys Arg Leu Lys Lys Lys Arg Arg Lys Ser Thr Ser Ser Ser Ser
470 475 480
Val Ser Ser Ala Asp Glu Ser Val Ser Ser Ser Ser Ser Ser
485 490 495
Ser Ser Gly His Lys Arg His Lys Lys His Lys Arg Asn Arg Ser
500 505 510
Glu Ser Ser Arg Ser Ser Arg Arg His Ser Ser Arg Ala Ser Ser
515 520 525
Asn Gln Ile Asp Gln Asn Arg Lys Asp Glu Cys Tyr Pro Val Pro
530 535 540
Ala Asn Thr Ser Ala Ser Phe Leu Asn His Lys Gln Glu Val Glu
545 550 555
Lys Leu Leu Gly Lys Gln Asp Arg Leu Gln Tyr Glu Lys Thr Gln
560 565 570
Ile Lys Glu Lys Asp Arg Cys Pro Leu Ser Ser Ser Ser Leu Glu
575 580 585
Ile Pro Asp Asp Phe Gly Val Tyr Ser Tyr Leu Phe Lys Lys Leu
590 595 600
Thr Ile Lys Gln Pro Gln Ala Gly Pro Ser Gly Asp Ile Pro Glu
605 610 615
Glu Gly Ile Val Ile Ile Asp Asp Ser Ser Ile His Val Thr Asp
620 625 630
Pro Glu Asp Leu Gln Val Gly Gln Asp Met Glu Val Glu Asp Ser
635 640 645
Gly Ile Asp Asp Pro Asp His Gly
650

```

&lt;210&gt; 35

&lt;211&gt; 144

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte ID No: 2804990CD1

&lt;400&gt; 35

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Met Leu Asn Arg Ile Ile Trp Leu Gln Ala Val Leu Glu Ile Ile
1 5 10 15
Thr Asn Lys Thr Thr Gln Ala Leu Thr Val Leu Ala Trp Gln Glu
20 25 30
Thr Leu Met Arg Asn Ala Ile Tyr Gln Asn Arg Leu Ala Leu Asp
35 40 45
Tyr Leu Leu Ala Ala Glu Gly Gly Val Cys Glu Lys Phe Asp Leu
50 55 60

```

```

Thr Asn Tyr Cys Leu His Ile Asp Asp Gln Gly Gln Val Val Glu
      65              70              75
Asp Ile Val Lys Asp Ile Thr Lys Leu Ala His Ala Pro Val Gln
      80              85              90
Val Trp His Gly Leu Asn Leu Gly Ala Met Phe Gly Asn Trp Phe
      95              100             105
Pro Ala Ile Gly Gly Phe Lys Thr Leu Ile Ile Arg Val Ile Ile
      110             115             120
Val Ile Gly Thr Cys Leu Leu Leu Pro Cys Leu Ile Pro Val Phe
      125             130             135
Leu Gln Met Ile Lys Asn Phe Val Ala
      140

```

```

<210> 36
<211> 424
<212> PRT
<213> Homo sapiens

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<220>
<221> misc_feature
<223> Incyte ID No: 168571CD1

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<400> 36
Met Ser Pro Leu Cys Ser Leu Cys Gln Glu Gly Ser Trp Thr Gly
  1      5      10      15
Pro Ala Ala Trp Met Pro Gly Pro Leu Gly Pro Glu His Gln Gly
      20      25      30
Val Gln Pro Arg Thr Pro Gln Ala Trp Ala Pro Leu Pro Ala Glu
      35      40      45
Gly Leu Trp Gly Ala Arg Gly Glu Ala Ser Arg His Gly Gly Cys
      50      55      60
Pro Ser Pro Ser His Gly Leu Gly Pro His Ala Ala Leu Cys Leu
      65      70      75
Pro Gln Glu Asn Pro Arg Leu Thr Glu Asp Phe Val Ser His Leu
      80      85      90
Glu Thr Glu Leu Glu Gln Ser Arg Leu Arg Glu Thr Glu Thr Leu
      95     100     105
Gly Ala Leu Arg Glu Met Gln Asp Lys Val Leu Asp Met Glu Lys
     110     115     120
Arg Asn Ser Ser Leu Pro Asp Glu Asn Asn Val Ala Gln Leu Gln
     125     130     135
Glu Glu Leu Lys Ala Leu Lys Val Arg Glu Gly Gln Ala Val Ala
     140     145     150
Ser Thr Arg Glu Leu Lys Leu Gln Leu Glu Leu Ser Asp Thr
     155     160     165
Trp Gln Ala His Leu Ala Arg Gly Gly Arg Trp Lys Glu Ser Pro
     170     175     180
Arg Lys Leu Val Val Gly Glu Leu Gln Asp Glu Leu Met Ser Val
     185     190     195
Arg Leu Arg Glu Ala Gln Ala Leu Ala Glu Gly Arg Glu Leu Arg
     200     205     210
Gln Arg Val Val Glu Leu Glu Thr Gln Asp His Ile His Arg Asn
     215     220     225
Leu Leu Asn Arg Val Glu Ala Glu Arg Ala Ala Leu Gln Glu Lys
     230     235     240
Leu Gln Tyr Leu Ala Ala Gln Asn Lys Gly Leu Gln Thr Gln Leu
     245     250     255
Ser Glu Ser Arg Arg Lys Gln Ala Glu Ala Glu Cys Lys Ser Lys
     260     265     270
Glu Glu Val Met Ala Val Arg Leu Arg Glu Ala Asp Ser Met Ala
     275     280     285
Ala Val Ala Glu Met Arg Gln Arg Ile Ala Glu Leu Glu Ile Gln
     290     295     300

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Arg	Glu	Glu	Gly	Arg	Ile	Gln	Gly	Gln	Leu	Asn	His	Ser	Asp	Ser	
				305					310					315	
Ser	Gln	Tyr	Ile	Arg	Glu	Leu	Lys	Asp	Gln	Ile	Glu	Glu	Leu	Lys	
				320					325					330	
Ala	Glu	Val	Arg	Leu	Leu	Lys	Gly	Pro	Pro	Pro	Phe	Glu	Asp	Pro	
				335					340					345	
Leu	Ala	Phe	Asp	Gly	Leu	Ser	Leu	Ala	Arg	His	Leu	Asp	Glu	Asp	
				350					355					360	
Ser	Leu	Pro	Ser	Ser	Asp	Glu	Glu	Leu	Leu	Gly	Val	Gly	Val	Gly	
				365					370					375	
Ala	Ala	Leu	Gln	Asp	Ala	Leu	Tyr	Pro	Leu	Ser	Pro	Arg	Asp	Ala	
				380					385					390	
Arg	Phe	Phe	Arg	Arg	Leu	Glu	Arg	Pro	Ala	Lys	Asp	Ser	Glu	Gly	
				395					400					405	
Ser	Ser	Asp	Ser	Asp	Ala	Asp	Glu	Leu	Ala	Ala	Pro	Tyr	Ser	Gln	
				410					415					420	
Gly	Leu	Asp	Asn												

&lt;210&gt; 37

&lt;211&gt; 1351

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte ID No: 1286391CD1

&lt;400&gt; 37

Met	Ala	Ala	Ala	Val	Pro	Lys	Ala	Glu	Asn	Pro	Ser	Arg	Thr	Gln	
1				5					10					15	
Val	Pro	Ser	Ala	Ala	Pro	Lys	Leu	Pro	Thr	Ser	Arg	Met	Met	Leu	
				20					25					30	
Ala	Val	His	Thr	Pro	Ala	Ala	Pro	Glu	Val	Pro	Leu	Ala	Pro		
				35					40					45	
Thr	Lys	Pro	Thr	Ala	Gln	Leu	Met	Ala	Thr	Ala	Gln	Lys	Thr	Val	
				50					55					60	
Val	Asn	Gln	Pro	Val	Leu	Val	Ala	Gln	Val	Glu	Pro	Thr	Thr	Pro	
				65					70					75	
Lys	Thr	Pro	Gln	Ala	Gln	Lys	Met	Pro	Val	Ala	Lys	Thr	Ser	Pro	
				80					85					90	
Ala	Gly	Pro	Lys	Thr	Pro	Lys	Ala	Gln	Ala	Gly	Pro	Ala	Ala	Thr	
				95					100					105	
Val	Ser	Lys	Ala	Pro	Ala	Ala	Ser	Lys	Ala	Pro	Ala	Ala	Pro	Lys	
				110					115					120	
Val	Pro	Val	Thr	Pro	Arg	Val	Ser	Arg	Ala	Pro	Lys	Thr	Pro	Ala	
				125					130					135	
Ala	Gln	Lys	Val	Pro	Thr	Asp	Ala	Gly	Pro	Thr	Leu	Asp	Val	Ala	
				140					145					150	
Arg	Leu	Leu	Ser	Glu	Val	Gln	Pro	Thr	Ser	Arg	Ala	Ser	Val	Ser	
				155					160					165	
Leu	Leu	Lys	Gly	Gln	Gly	Gln	Ala	Gly	Arg	Gln	Gly	Pro	Gln	Ser	
				170					175					180	
Ser	Gly	Thr	Leu	Ala	Leu	Ser	Ser	Lys	His	Gln	Phe	Gln	Met	Glu	
				185					190					195	
Gly	Leu	Leu	Gly	Ala	Trp	Glu	Gly	Ala	Pro	Arg	Gln	Pro	Pro	Arg	
				200					205					210	
His	Leu	Gln	Ala	Asn	Ser	Thr	Val	Thr	Ser	Phe	Gln	Arg	Tyr	His	
				215					220					225	
Glu	Ala	Leu	Asn	Thr	Pro	Phe	Glu	Leu	Asn	Leu	Ser	Gly	Glu	Pro	
				230					235					240	
Gly	Asn	Gln	Gly	Leu	Arg	Arg	Val	Val	Ile	Asp	Gly	Ser	Ser	Val	
				245					250					255	

Ala Met Val His Gly Leu Gln His Phe Phe Ser Cys Arg Gly Ile	260	265	270
Ala Met Ala Val Gln Phe Phe Trp Asn Arg Gly His Arg Glu Val	275	280	285
Thr Val Phe Val Pro Thr Trp Gln Leu Lys Lys Asn Arg Arg Val	290	295	300
Arg Glu Ser His Phe Leu Thr Lys Leu His Ser Leu Lys Met Leu	305	310	315
Ser Ile Thr Pro Ser Gln Leu Glu Asn Gly Lys Lys Ile Thr Thr	320	325	330
Tyr Asp Tyr Arg Phe Met Val Lys Leu Ala Glu Glu Thr Asp Gly	335	340	345
Ile Ile Val Thr Asn Glu Gln Ile His Ile Leu Met Asn Ser Ser	350	355	360
Lys Lys Leu Met Val Lys Asp Arg Leu Leu Pro Phe Thr Phe Ala	365	370	375
Gly Asn Leu Phe Met Val Pro Asp Asp Pro Leu Gly Arg Asp Gly	380	385	390
Pro Thr Leu Asp Glu Phe Leu Lys Lys Pro Asn Arg Leu Asp Thr	395	400	405
Asp Ile Gly Asn Phe Leu Lys Val Trp Lys Thr Leu Pro Pro Ser	410	415	420
Ser Ala Ser Val Thr Glu Leu Ser Asp Asp Ala Asp Ser Gly Pro	425	430	435
Leu Glu Ser Leu Pro Asn Met Glu Glu Val Arg Glu Glu Lys Glu	440	445	450
Glu Arg Gln Asp Glu Glu Gln Arg Gln Gly Gln Gly Thr Gln Lys	455	460	465
Ala Ala Glu Glu Asp Asp Leu Asp Ser Ser Leu Ala Ser Val Phe	470	475	480
Arg Val Glu Cys Pro Ser Leu Ser Glu Glu Ile Leu Arg Cys Leu	485	490	495
Ser Leu His Asp Pro Pro Asp Gly Ala Leu Asp Ile Asp Leu Leu	500	505	510
Pro Gly Ala Ala Ser Pro Tyr Leu Gly Ile Pro Trp Asp Gly Lys	515	520	525
Ala Pro Cys Gln Gln Val Leu Ala His Leu Ala Gln Leu Thr Ile	530	535	540
Pro Ser Asn Phe Thr Ala Leu Ser Phe Phe Met Gly Phe Met Asp	545	550	555
Ser His Arg Asp Ala Ile Pro Asp Tyr Glu Ala Leu Val Gly Pro	560	565	570
Leu His Ser Leu Leu Lys Gln Lys Pro Asp Trp Gln Trp Asp Gln	575	580	585
Glu His Glu Glu Ala Phe Leu Ala Leu Lys Arg Ala Leu Val Ser	590	595	600
Ala Leu Cys Leu Met Ala Pro Asn Ser Gln Leu Pro Phe Arg Leu	605	610	615
Glu Val Thr Val Ser His Val Ala Leu Thr Ala Ile Leu His Gln	620	625	630
Glu His Ser Gly Arg Lys His Pro Ile Ala Tyr Thr Ser Lys Pro	635	640	645
Leu Leu Pro Asp Glu Glu Ser Gln Gly Pro Gln Ser Gly Gly Asp	650	655	660
Ser Pro Tyr Ala Val Ala Trp Ala Leu Lys His Phe Ser Arg Cys	665	670	675
Ile Gly Asp Thr Pro Val Val Leu Asp Leu Ser Tyr Ala Ser Arg	680	685	690
Thr Thr Ala Asp Pro Glu Val Arg Glu Gly Arg Arg Val Ser Lys	695	700	705
Ala Trp Leu Ile Arg Trp Ser Leu Leu Val Gln Asp Lys Gly Lys	710	715	720
Arg Ala Leu Glu Leu Ala Leu Leu Gln Gly Leu Leu Gly Glu Asn			

725	730	735
Arg Leu Leu Thr Pro Ala Ala Ser Met	Pro Arg Phe Phe Gln Val	
740	745	750
Leu Pro Pro Phe Ser Asp Leu Ser Thr	Phe Val Cys Ile His Met	
755	760	765
Ser Gly Tyr Cys Phe Tyr Arg Glu Asp	Glu Trp Cys Ala Gly Phe	
770	775	780
Gly Leu Tyr Val Leu Ser Pro Thr Ser	Pro Pro Val Ser Leu Ser	
785	790	795
Phe Ser Cys Ser Pro Tyr Thr Pro Thr	Tyr Ala His Leu Ala Ala	
800	805	810
Val Ala Cys Gly Leu Glu Arg Phe Gly	Gln Ser Pro Leu Pro Val	
815	820	825
Val Phe Leu Thr His Cys Asn Trp Ile	Phe Ser Leu Leu Trp Glu	
830	835	840
Leu Leu Pro Leu Trp Arg Ala Arg Gly	Phe Leu Ser Ser Asp Gly	
845	850	855
Ala Pro Leu Pro His Pro Ser Leu Leu	Ser Tyr Ile Ile Ser Leu	
860	865	870
Thr Ser Gly Leu Ser Ser Leu Pro Phe	Ile Tyr Arg Thr Ser Tyr	
875	880	885
Arg Gly Ser Leu Phe Ala Val Thr Val	Asp Thr Leu Ala Lys Gln	
890	895	900
Gly Ala Gln Gly Gly Gly Gln Trp Trp	Ser Leu Pro Lys Asp Val	
905	910	915
Pro Ala Pro Thr Val Ser Pro His Ala	Met Gly Lys Arg Pro Asn	
920	925	930
Leu Leu Ala Leu Gln Leu Ser Asp Ser	Thr Leu Ala Asp Ile Ile	
935	940	945
Ala Arg Leu Gln Ala Gly Gln Lys Leu	Ser Gly Ser Ser Pro Phe	
950	955	960
Ser Ser Ala Phe Asn Ser Leu Ser Leu	Asp Lys Glu Ser Gly Leu	
965	970	975
Leu Met Phe Lys Gly Asp Lys Lys Pro	Arg Val Trp Val Val Pro	
980	985	990
Thr Gln Leu Arg Arg Asp Leu Ile Phe	Ser Val His Asp Ile Pro	
995	1000	1005
Leu Gly Ala His Gln Arg Pro Glu Glu	Thr Tyr Lys Lys Leu Arg	
1010	1015	1020
Leu Leu Gly Trp Trp Pro Gly Met Gln	Glu His Val Lys Asp Tyr	
1025	1030	1035
Cys Arg Ser Cys Leu Phe Cys Ile Pro	Arg Asn Leu Ile Gly Ser	
1040	1045	1050
Glu Leu Lys Val Ile Glu Ser Pro Trp	Pro Leu Arg Ser Thr Ala	
1055	1060	1065
Pro Trp Ser Asn Leu Gln Ile Glu Val	Val Gly Pro Val Thr Ile	
1070	1075	1080
Ser Glu Glu Gly His Lys His Val Leu	Ile Val Ala Asp Pro Asn	
1085	1090	1095
Thr Arg Trp Val Glu Ala Phe Pro Leu	Lys Pro Tyr Thr His Thr	
1100	1105	1110
Ala Val Ala Gln Val Leu Leu Gln His	Val Phe Ala Arg Trp Gly	
1115	1120	1125
Val Pro Val Arg Leu Glu Ala Ala Gln	Gly Pro Gln Phe Ala Arg	
1130	1135	1140
His Val Leu Val Ser Cys Gly Leu Ala	Leu Gly Ala Gln Val Ala	
1145	1150	1155
Ser Leu Ser Arg Asp Leu Gln Phe Pro	Cys Leu Thr Ser Ser Gly	
1160	1165	1170
Ala Tyr Trp Glu Phe Lys Arg Ala Leu	Lys Glu Phe Ile Phe Leu	
1175	1180	1185
His Gly Lys Lys Trp Ala Ala Ser Leu	Pro Leu Leu His Leu Ala	
1190	1195	1200

Phe Arg Ala Ser Ser Thr Asp Ala Thr Pro Phe Lys Val Leu Thr  
 1205 1210 1215  
 Gly Gly Glu Ser Arg Leu Thr Glu Pro Leu Trp Trp Glu Met Ser  
 1220 1225 1230  
 Ser Ala Asn Ile Glu Gly Leu Lys Met Asp Val Phe Leu Leu Gln  
 1235 1240 1245  
 Leu Val Gly Glu Leu Leu Glu Leu His Trp Arg Val Ala Asp Lys  
 1250 1255 1260  
 Ala Ser Glu Lys Ala Glu Asn Arg Arg Phe Lys Arg Glu Ser Gln  
 1265 1270 1275  
 Glu Lys Glu Trp Asn Val Gly Asp Gln Val Leu Leu Leu Ser Leu  
 1280 1285 1290  
 Pro Arg Asn Gly Ser Ser Ala Lys Trp Val Gly Pro Phe Tyr Ile  
 1295 1300 1305  
 Gly Asp Arg Leu Ser Leu Ser Leu Tyr Arg Ile Trp Gly Phe Pro  
 1310 1315 1320  
 Thr Pro Glu Lys Leu Gly Cys Ile Tyr Pro Ser Ser Leu Met Lys  
 1325 1330 1335  
 Ala Phe Ala Lys Ser Gly Thr Pro Leu Ser Phe Lys Val Leu Glu  
 1340 1345 1350  
 Gln

<210> 38  
 <211> 78  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte ID No: 2007684CD1

<400> 38  
 Met Gln Glu Met Val Arg Glu Leu Trp Met Trp Asn Val Glu Glu  
 1 5 10 15  
 Glu Glu His Glu Val Gly Ile Cys Thr Trp Gly Gly Gln His Cys  
 20 25 30  
 Gly Cys Pro Ala Lys Ser Leu Pro Gly Pro His Pro Gly Gly Val  
 35 40 45  
 Ser Ala Pro Gln Ser Ala Ser Gln Leu Met Val Lys Leu Leu Val  
 50 55 60  
 Trp Gln Lys Ser Val His Lys Leu Arg Lys Leu Leu Glu Lys Thr  
 65 70 75  
 Glu Asn Tyr

<210> 39  
 <211> 411  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte ID No: 2227040CD1

<400> 39  
 Met Thr Glu Met Ser Glu Lys Glu Asn Glu Pro Asp Asp Ala Ala  
 1 5 10 15  
 Thr His Ser Pro Pro Gly Thr Val Ser Ala Leu Gln Glu Thr Lys  
 20 25 30  
 Leu Gln Arg Phe Lys Arg Ser Leu Ser Leu Lys Thr Ile Leu Arg  
 35 40 45  
 Ser Lys Ser Leu Glu Asn Phe Phe Leu Arg Ser Gly Ser Glu Leu



	50		55		60
Lys Cys Pro Thr	Glu Val Leu Leu Thr	Pro Pro Thr Pro Leu Pro			
	65		70		75
Pro Pro Ser Pro	Pro Pro Thr Ala Ser	Asp Arg Gly Leu Ala Thr			
	80		85		90
Pro Ser Pro Ser	Pro Cys Pro Val Pro Arg	Pro Leu Ala Ala Leu			
	95		100		105
Lys Pro Val Thr	Leu His Ser Phe Gln	Glu His Val Phe Lys Arg			
	110		115		120
Ala Ser Pro Cys	Glu Leu Cys His Gln	Leu Ile Val Gly Asn Ser			
	125		130		135
Lys Gln Gly Leu	Arg Cys Lys Met Cys	Lys Val Ser Val His Leu			
	140		145		150
Trp Cys Ser Glu	Glu Ile Ser His Gln	Gln Cys Pro Gly Lys Thr			
	155		160		165
Ser Thr Ser Phe	Arg Arg Asn Phe Ser	Ser Pro Leu Leu Val His			
	170		175		180
Glu Pro Pro Pro	Val Cys Ala Thr Ser	Lys Glu Ser Pro Pro Thr			
	185		190		195
Gly Asp Ser Gly	Lys Val Asp Pro Val	Tyr Glu Thr Leu Arg Tyr			
	200		205		210
Gly Thr Ser Leu	Ala Leu Met Asn Arg	Ser Ser Phe Ser Ser Thr			
	215		220		225
Ser Glu Ser Pro	Thr Arg Ser Leu Ser	Glu Arg Asp Glu Leu Thr			
	230		235		240
Glu Asp Gly Glu	Gly Ser Ile Arg Ser	Ser Glu Glu Gly Pro Gly			
	245		250		255
Asp Ser Ala Ser	Pro Val Phe Thr Ala	Pro Ala Glu Ser Glu Gly			
	260		265		270
Pro Gly Pro Glu	Glu Lys Ser Pro Gly	Gln Gln Leu Pro Lys Ala			
	275		280		285
Thr Leu Arg Lys	Asp Val Gly Pro Met	Tyr Ser Tyr Val Ala Leu			
	290		295		300
Tyr Lys Phe Leu	Pro Gln Glu Asn Asn	Asp Leu Ala Leu Gln Pro			
	305		310		315
Gly Asp Arg Ile	Met Leu Val Asp Asp	Ser Asn Glu Asp Trp Trp			
	320		325		330
Lys Gly Lys Ile	Gly Asp Arg Val Gly	Phe Phe Pro Ala Asn Phe			
	335		340		345
Val Gln Arg Val	Arg Pro Gly Glu Asn	Val Trp Arg Cys Cys Gln			
	350		355		360
Pro Phe Ser Gly	Asn Lys Glu Gln Gly	Tyr Met Ser Leu Lys Glu			
	365		370		375
Asn Gln Ile Cys	Val Gly Val Gly Arg	Ser Lys Asp Ala Asp Gly			
	380		385		390
Phe Ile Arg Val	Ser Ser Gly Lys Lys	Arg Gly Leu Val Pro Val			
	395		400		405
Asp Ala Leu Thr	Glu Ile				
	410				

&lt;210&gt; 40

&lt;211&gt; 1704

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte ID No: 4346130CD1

&lt;400&gt; 40

Met Ser Ser Val Ser Glu Val Asn Val Asp Ile Lys Asp Phe Leu

1

5

10

15

Met Ser Ile Asn Leu Glu Gln Tyr Leu Leu His Phe His Glu Ser

				20					25					30
Gly	Phe	Thr	Thr	Val	Lys	Asp	Cys	Ala	Ala	Ile	Asn	Asp	Ser	Leu
				35					40					45
Leu	Gln	Lys	Ile	Gly	Ile	Ser	Pro	Thr	Gly	His	Arg	Arg	Arg	Ile
				50					55					60
Leu	Lys	Gln	Leu	Gln	Ile	Ile	Leu	Ser	Lys	Met	Gln	Asp	Ile	Pro
				65					70					75
Ile	Tyr	Ala	Asn	Val	His	Lys	Thr	Lys	Lys	Asn	Asp	Asp	Pro	Ser
				80					85					90
Lys	Asp	Tyr	His	Val	Pro	Ser	Ser	Asp	Gln	Asn	Ile	Cys	Ile	Glu
				95					100					105
Leu	Ser	Asn	Ser	Gly	Ser	Val	Gln	Thr	Ser	Ser	Pro	Pro	Gln	Leu
				110					115					120
Glu	Thr	Val	Arg	Lys	Asn	Leu	Glu	Asp	Ser	Asp	Ala	Ser	Val	Glu
				125					130					135
Arg	Ser	Gln	Tyr	Pro	Gln	Ser	Asp	Asp	Lys	Leu	Ser	Pro	Pro	Lys
				140					145					150
Arg	Asp	Phe	Pro	Thr	Ala	Glu	Glu	Pro	His	Leu	Asn	Leu	Gly	Ser
				155					160					165
Leu	Asn	Asp	Ser	Leu	Phe	Gly	Ser	Asp	Asn	Ile	Lys	Ile	Glu	Ser
				170					175					180
Leu	Ile	Thr	Lys	Lys	Thr	Val	Asp	His	Thr	Val	Glu	Glu	Gln	Gln
				185					190					195
Thr	Glu	Lys	Val	Lys	Leu	Ile	Thr	Glu	Asn	Leu	Ser	Lys	Leu	Pro
				200					205					210
Asn	Ala	Asp	Ser	Glu	Cys	Leu	Ser	Phe	Val	Gly	Cys	Ser	Thr	Ser
				215					220					225
Gly	Thr	Asn	Ser	Gly	Asn	Gly	Thr	Asn	Gly	Leu	Leu	Glu	Gly	Ser
				230					235					240
Pro	Pro	Ser	Pro	Phe	Phe	Lys	Phe	Gln	Gly	Glu	Met	Ile	Val	Asn
				245					250					255
Asp	Leu	Tyr	Val	Pro	Ser	Ser	Pro	Ile	Leu	Ala	Pro	Val	Arg	Ser
				260					265					270
Arg	Ser	Lys	Leu	Val	Ser	Arg	Pro	Ser	Arg	Ser	Phe	Leu	Leu	Arg
				275					280					285
His	Arg	Pro	Val	Pro	Glu	Ile	Pro	Gly	Ser	Thr	Lys	Gly	Val	Ser
				290					295					300
Gly	Ser	Tyr	Phe	Arg	Glu	Arg	Arg	Asn	Val	Ala	Thr	Ser	Thr	Glu
				305					310					315
Lys	Ser	Val	Ala	Trp	Gln	Asn	Ser	Asn	Glu	Glu	Asn	Ser	Ser	Ser
				320					325					330
Ile	Phe	Pro	Tyr	Gly	Glu	Thr	Phe	Leu	Phe	Gln	Arg	Leu	Glu	Asn
				335					340					345
Ser	Lys	Lys	Arg	Ser	Ile	Lys	Asn	Glu	Phe	Leu	Thr	Gln	Gly	Glu
				350					355					360
Ala	Leu	Lys	Gly	Glu	Ala	Ala	Thr	Ala	Thr	Asn	Ser	Phe	Ile	Ile
				365					370					375
Lys	Ser	Ser	Ile	Tyr	Asp	Asn	Arg	Lys	Glu	Lys	Ile	Ser	Glu	Asp
				380					385					390
Lys	Val	Glu	Asp	Ile	Trp	Ile	Pro	Arg	Glu	Asp	Lys	Asn	Asn	Phe
				395					400					405
Leu	Ile	Asp	Thr	Ala	Ser	Glu	Ser	Glu	Tyr	Ser	Thr	Val	Glu	Glu
				410					415					420
Cys	Phe	Gln	Ser	Leu	Arg	Arg	Lys	Asn	Ser	Lys	Ala	Ser	Lys	Ser
				425					430					435
Arg	Thr	Gln	Lys	Ala	Leu	Ile	Leu	Asp	Ser	Val	Asn	Arg	His	Ser
				440					445					450
Tyr	Pro	Leu	Ser	Ser	Thr	Ser	Gly	Asn	Ala	Asp	Ser	Ser	Ala	Val
				455					460					465
Ser	Ser	Gln	Ala	Ile	Ser	Pro	Tyr	Ala	Cys	Phe	Tyr	Gly	Ala	Ser
				470					475					480
Ala	Lys	Lys	Val	Lys	Ser	Gly	Trp	Leu	Asp	Lys	Leu	Ser	Pro	Gln
				485					490					495

Gly Lys Arg Met	Phe Gln Lys Arg Trp Val Lys Phe Asp Gly Leu	
500	505	510
Ser Ile Ser Tyr	Tyr Asn Asn Glu Lys Glu Met Tyr Ser Lys Gly	
515	520	525
Ile Ile Pro Leu	Ser Ala Ile Ser Thr Val Arg Val Gln Gly Asp	
530	535	540
Asn Lys Phe Glu	Val Val Thr Thr Gln Arg Thr Phe Val Phe Arg	
545	550	555
Val Glu Lys Glu	Glu Glu Arg Asn Asp Trp Ile Ser Ile Leu Leu	
560	565	570
Asn Ala Leu Lys	Ser Gln Ser Leu Thr Ser Gln Ser Gln Ala Val	
575	580	585
Val Thr Pro Glu	Lys Cys Gly Tyr Leu Glu Leu Arg Gly Tyr Lys	
590	595	600
Ala Lys Ile Phe	Thr Val Leu Ser Gly Asn Ser Val Trp Leu Cys	
605	610	615
Lys Asn Glu Gln	Asp Phe Lys Ser Gly Leu Gly Ile Thr Ile Ile	
620	625	630
Pro Met Asn Val	Ala Asn Val Lys Gln Val Asp Arg Thr Val Lys	
635	640	645
Gln Ser Phe Glu	Ile Ile Thr Pro Tyr Arg Ser Phe Ser Phe Thr	
650	655	660
Ala Glu Thr Glu	Lys Glu Lys Gln Asp Trp Ile Glu Ala Val Gln	
665	670	675
Gln Ser Ile Ala	Glu Thr Leu Ser Asp Tyr Glu Val Ala Glu Lys	
680	685	690
Ile Trp Phe Asn	Glu Ser Asn Arg Ser Cys Ala Asp Cys Lys Ala	
695	700	705
Pro Asp Pro Asp	Trp Ala Ser Ile Asn Leu Cys Val Val Ile Cys	
710	715	720
Lys Lys Cys Ala	Gly Gln His Arg Ser Leu Gly Pro Lys Asp Ser	
725	730	735
Lys Val Arg Ser	Leu Lys Met Asp Ala Ser Ile Trp Ser Asn Glu	
740	745	750
Leu Ile Glu Leu	Phe Ile Val Ile Gly Asn Lys Arg Ala Asn Asp	
755	760	765
Phe Trp Ala Gly	Asn Leu Gln Lys Asp Glu Glu Leu His Met Asp	
770	775	780
Ser Pro Val Glu	Lys Arg Lys Asn Phe Ile Thr Gln Lys Tyr Lys	
785	790	795
Glu Gly Lys Phe	Arg Lys Thr Leu Leu Ala Ser Leu Thr Lys Glu	
800	805	810
Glu Leu Asn Lys	Ala Leu Cys Ala Ala Val Val Lys Pro Asp Val	
815	820	825
Leu Glu Thr Met	Ala Leu Leu Phe Ser Gly Ala Asp Val Met Cys	
830	835	840
Ala Thr Gly Asp	Pro Val His Ser Thr Pro Tyr Leu Leu Ala Lys	
845	850	855
Lys Ala Gly Gln	Ser Leu Gln Met Glu Phe Leu Tyr His Asn Lys	
860	865	870
Phe Ser Asp Phe	Pro Gln His Asp Ile His Ser Glu Gly Val Leu	
875	880	885
Ser Gln Glu Ser	Ser Gln Ser Thr Phe Leu Cys Asp Phe Leu Tyr	
890	895	900
Gln Ala Pro Ser	Ala Ala Ser Lys Leu Ser Ser Glu Lys Lys Leu	
905	910	915
Leu Glu Glu Thr	Asn Lys Lys Trp Cys Val Leu Glu Gly Gly Phe	
920	925	930
Leu Ser Tyr Tyr	Glu Asn Asp Lys Ser Thr Thr Pro Asn Gly Thr	
935	940	945
Ile Asn Ile Asn	Glu Val Ile Cys Leu Ala Ile His Lys Glu Asp	
950	955	960
Phe Tyr Leu Asn	Thr Gly Pro Ile Phe Ile Phe Glu Ile Tyr Leu	

965	970	975
Pro Ser Glu Arg Val Phe Leu Phe Gly Ala Glu Thr Ser Gln Ala		
980	985	990
Gln Arg Lys Trp Thr Glu Ala Ile Ala Lys His Phe Val Pro Leu		
995	1000	1005
Phe Ala Glu Asn Leu Thr Glu Ala Asp Tyr Asp Leu Ile Gly Gln		
1010	1015	1020
Leu Phe Tyr Lys Asp Cys His Ala Leu Asp Gln Trp Arg Lys Gly		
1025	1030	1035
Trp Phe Ala Met Asp Lys Ser Ser Leu His Phe Cys Leu Gln Met		
1040	1045	1050
Gln Glu Val Gln Gly Asp Arg Met His Leu Arg Arg Leu Gln Glu		
1055	1060	1065
Leu Thr Ile Ser Thr Met Val Gln Asn Gly Glu Lys Leu Asp Val		
1070	1075	1080
Leu Leu Leu Val Glu Lys Gly Arg Thr Leu Tyr Ile His Gly His		
1085	1090	1095
Thr Lys Leu Asp Phe Thr Val Trp His Thr Ala Ile Glu Lys Ala		
1100	1105	1110
Ala Gly Thr Asp Gly Asn Ala Leu Gln Asp Gln Gln Leu Ser Lys		
1115	1120	1125
Asn Asp Val Pro Ile Ile Val Asn Ser Cys Ile Ala Phe Val Thr		
1130	1135	1140
Gln Tyr Gly Leu Gly Cys Lys Tyr Ile Tyr Gln Lys Asn Gly Asp		
1145	1150	1155
Pro Leu His Ile Ser Glu Leu Leu Glu Ser Phe Lys Lys Asp Ala		
1160	1165	1170
Arg Ser Phe Lys Leu Arg Ala Gly Lys His Gln Leu Glu Asp Val		
1175	1180	1185
Thr Ala Val Leu Lys Ser Phe Leu Ser Asp Ile Asp Asp Ala Leu		
1190	1195	1200
Leu Thr Lys Glu Leu Tyr Pro Tyr Trp Ile Ser Ala Leu Asp Thr		
1205	1210	1215
Gln Asp Asp Lys Glu Arg Ile Lys Lys Tyr Gly Ala Phe Ile Arg		
1220	1225	1230
Ser Leu Pro Gly Val Asn Arg Ala Thr Leu Ala Ala Ile Ile Glu		
1235	1240	1245
His Leu Tyr Arg Val Gln Lys Cys Ser Glu Ile Asn His Met Asn		
1250	1255	1260
Ala His Asn Leu Ala Leu Val Phe Ser Ser Cys Leu Phe Gln Thr		
1265	1270	1275
Lys Gly Gln Thr Ser Glu Glu Val Asn Val Ile Glu Asp Leu Ile		
1280	1285	1290
Asn Asn Tyr Val Glu Ile Phe Glu Val Lys Glu Asp Gln Val Lys		
1295	1300	1305
Gln Met Asp Ile Glu Asn Ser Phe Ile Thr Lys Trp Lys Asp Thr		
1310	1315	1320
Gln Val Ser Gln Ala Gly Asp Leu Leu Ile Glu Val Tyr Val Glu		
1325	1330	1335
Arg Lys Glu Pro Asp Cys Ser Ile Ile Arg Ile Ser Pro Val		
1340	1345	1350
Met Glu Ala Glu Glu Leu Thr Asn Asp Ile Leu Ala Ile Lys Asn		
1355	1360	1365
Ile Ile Pro Thr Lys Gly Asp Ile Trp Ala Thr Phe Glu Val Ile		
1370	1375	1380
Glu Asn Glu Glu Leu Glu Arg Pro Leu His Tyr Lys Glu Asn Val		
1385	1390	1395
Leu Glu Gln Val Leu Arg Trp Ser Ser Leu Ala Glu Pro Gly Ser		
1400	1405	1410
Ala Tyr Leu Val Val Lys Arg Phe Leu Thr Ala Asp Thr Ile Lys		
1415	1420	1425
His Cys Ser Asp Arg Ser Thr Leu Gly Ser Ile Lys Glu Gly Ile		
1430	1435	1440

Leu Lys Ile Lys Glu Glu Pro Ser Lys Ile Leu Ser Gly Asn Lys  
 1445 1450 1455  
 Phe Gln Asp Arg Tyr Phe Val Leu Arg Asp Gly Phe Leu Phe Leu  
 1460 1465 1470  
 Tyr Lys Asp Val Lys Ser Ser Lys His Asp Lys Met Phe Ser Leu  
 1475 1480 1485  
 Ser Ser Met Lys Phe Tyr Arg Gly Val Lys Lys Lys Met Lys Pro  
 1490 1495 1500  
 Pro Thr Ser Trp Gly Leu Thr Ala Tyr Ser Glu Lys His His Trp  
 1505 1510 1515  
 His Leu Cys Cys Asp Ser Ser Gln Thr Gln Thr Glu Trp Met Thr  
 1520 1525 1530  
 Ser Ile Phe Ile Ala Gln His Glu Tyr Asp Ile Trp Pro Pro Ala  
 1535 1540 1545  
 Gly Lys Glu Arg Lys Arg Ser Ile Thr Lys Asn Pro Lys Ile Gly  
 1550 1555 1560  
 Gly Leu Pro Leu Ile Pro Ile Gln His Glu Gly Asn Ala Thr Leu  
 1565 1570 1575  
 Ala Arg Lys Asn Ile Glu Ser Ala Arg Ala Glu Leu Glu Arg Leu  
 1580 1585 1590  
 Arg Leu Ser Glu Lys Cys Asp Lys Glu Ser Val Asp Ser Ser Leu  
 1595 1600 1605  
 Lys Glu Arg Ala Ser Met Val Ala His Cys Leu Glu His Lys Asp  
 1610 1615 1620  
 Asp Lys Leu Arg Asn Arg Pro Arg Lys His Arg Ser Phe Asn Cys  
 1625 1630 1635  
 Leu Glu Asp Thr Glu Pro Glu Ala Pro Leu Gly Gln Pro Lys Gly  
 1640 1645 1650  
 His Lys Gly Leu Lys Thr Leu Arg Lys Thr Glu Asp Arg Asn Ser  
 1655 1660 1665  
 Lys Ala Thr Leu Asp Ser Asp His Lys Leu Pro Ser Arg Val Ile  
 1670 1675 1680  
 Glu Glu Leu Asn Val Val Leu Gln Arg Ser Arg Thr Leu Pro Lys  
 1685 1690 1695  
 Glu Leu Gln Asp Glu Gln Ile Leu Lys  
 1700

<210> 41  
 <211> 243  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte ID No: 55117040CD1

<400> 41  
 Met Val Ala Glu Val Asp Ser Met Pro Ala Ala Ser Ser Val Lys  
 1 5 10 15  
 Lys Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys Cys His  
 20 25 30  
 Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val Gly Thr  
 35 40 45  
 Ser Gly Asp His Asn Asp Ser Ser Val Lys Thr Leu Gly Ser Lys  
 50 55 60  
 Arg Cys Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser  
 65 70 75  
 Gly Lys Ser Asn Val Val Ala Trp Gly Asp Tyr Asp Asp Ser Ala  
 80 85 90  
 Phe Met Asp Pro Arg Tyr His Val His Gly Glu Asp Leu Asp Lys  
 95 100 105  
 Leu His Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp Leu  
 110 115 120

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Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys Arg Asp Lys Gln
      125                      130                      135
Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu
      140                      145                      150
Val Val Lys Leu Val Leu Asp Arg Arg Cys Gln Leu Asn Val Leu
      155                      160                      165
Asp Asn Lys Lys Arg Thr Ala Leu Thr Lys Ala Val Gln Cys Gln
      170                      175                      180
Glu Asp Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro
      185                      190                      195
Asn Ile Pro Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Val
      200                      205                      210
Tyr Asn Glu Asp Lys Leu Met Ala Lys His Cys Ser Tyr Thr Val
      215                      220                      225
Leu Ile Ser Asn Gln Lys Thr Ala Trp Pro His Thr Thr Ala Thr
      230                      235                      240
Trp Tyr Thr

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<210> 42
<211> 248
<212> PRT
<213> Homo sapiens

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<220>
<221> misc_feature
<223> Incyte ID No: 7472392CD1

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<400> 42
Met Asp Val Leu His Ala Ser Val Arg Arg Ser Thr Ile Val Cys
  1      5      10      15
Met Glu Glu Thr Glu Phe Leu Val Val Asp Arg Glu Asp Phe Phe
      20      25      30
Ala Asn Lys Leu Asp Gln Glu Val Gln Lys Asp Ala Gln Tyr Arg
      35      40      45
Phe Glu Phe Phe Arg Lys Met Glu Leu Phe Ala Ser Trp Ser Asp
      50      55      60
Glu Lys Leu Trp Gln Leu Val Ala Met Ala Lys Ile Glu Arg Phe
      65      70      75
Ser Tyr Gly Gln Leu Ile Ser Lys Asp Phe Gly Glu Ser Pro Phe
      80      85      90
Ile Met Phe Ile Ser Lys Gly Ser Cys Glu Val Leu Arg Leu Leu
      95     100     105
Asp Leu Gly Ala Ser Pro Ser Tyr Arg Arg Trp Ile Trp Gln His
     110     115     120
Leu Glu Leu Ile Asp Gly Arg Pro Leu Lys Thr His Leu Ser Glu
     125     130     135
Tyr Ser Pro Met Glu Arg Phe Lys Glu Phe Gln Ile Lys Ser Tyr
     140     145     150
Pro Leu Gln Asp Phe Ser Ser Leu Lys Leu Pro His Leu Lys Lys
     155     160     165
Ala Trp Gly Leu Gln Gly Thr Ser Phe Ser Arg Lys Ile Arg Thr
     170     175     180
Ser Gly Asp Thr Leu Pro Lys Met Leu Gly Pro Lys Ile Gln Ser
     185     190     195
Arg Pro Ala Gln Ser Ile Lys Cys Ala Met Ile Asn Ile Lys Pro
     200     205     210
Gly Glu Leu Pro Lys Glu Ala Ala Val Gly Ala Tyr Val Lys Val
     215     220     225
His Thr Val Glu Gln Gly Glu Ile Leu Val Ser Val Pro Arg Ala
     230     235     240
Leu Phe Thr Met Glu Tyr Val Thr
     245

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<210> 43  
 <211> 310  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte ID No: 4028960CD1

<400> 43  
 Met Gly Lys Arg Arg Cys Val Pro Pro Leu Glu Pro Lys Leu Ala  
 1 5 10 15  
 Ala Gly Cys Cys Gly Val Lys Lys Pro Lys Leu Ser Gly Ser Gly  
 20 25 30  
 Thr His Ser His Gly Asn Gln Ser Thr Thr Val Pro Gly Ser Ser  
 35 40 45  
 Ser Gly Pro Leu Gln Asn His Gln His Val Asp Ser Ser Ser Gly  
 50 55 60  
 Arg Glu Asn Val Ser Asp Leu Thr Leu Gly Pro Gly Asn Ser Pro  
 65 70 75  
 Ile Thr Arg Met Asn Pro Ala Ser Gly Ala Leu Ser Pro Leu Pro  
 80 85 90  
 Arg Pro Asn Gly Thr Ala Asn Thr Thr Lys Asn Leu Val Val Thr  
 95 100 105  
 Ala Glu Met Cys Cys Tyr Cys Phe Asp Val Leu Tyr Cys His Leu  
 110 115 120  
 Tyr Gly Phe Pro Gln Pro Arg Leu Pro Arg Phe Thr Asn Asp Pro  
 125 130 135  
 Tyr Pro Leu Phe Val Thr Trp Lys Thr Gly Arg Asp Lys Arg Leu  
 140 145 150  
 Arg Gly Cys Ile Gly Thr Phe Ser Ala Met Asn Leu His Ser Gly  
 155 160 165  
 Leu Arg Glu Tyr Thr Leu Thr Ser Ala Leu Lys Asp Ser Arg Phe  
 170 175 180  
 Pro Pro Leu Thr Arg Glu Glu Leu Pro Lys Leu Phe Cys Ser Val  
 185 190 195  
 Ser Leu Leu Thr Asn Phe Glu Asp Ala Ser Asp Tyr Leu Asp Trp  
 200 205 210  
 Glu Val Gly Val His Gly Ile Arg Ile Glu Phe Ile Asn Glu Lys  
 215 220 225  
 Gly Val Lys Arg Thr Ala Thr Tyr Leu Pro Glu Val Ala Lys Glu  
 230 235 240  
 Gln Asp Trp Asp Gln Ile Gln Thr Ile Asp Ser Leu Leu Arg Lys  
 245 250 255  
 Gly Gly Phe Lys Ala Pro Ile Thr Ser Glu Phe Arg Lys Thr Ile  
 260 265 270  
 Lys Leu Thr Arg Tyr Arg Ser Glu Lys Val Thr Ile Ser Tyr Ala  
 275 280 285  
 Glu Tyr Ile Ala Ser Arg Gln His Cys Phe Gln Asn Gly Thr Leu  
 290 295 300  
 His Ala Pro Pro Leu Tyr Asn His Tyr Ser  
 305 310

<210> 44  
 <211> 838  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte ID No: 8227004CD1

<400> 44

Met	Phe	Trp	Lys	Phe	Asp	Leu	His	Ser	Ser	Ser	His	Ile	Asp	Thr
1				5					10					15
Leu	Leu	Glu	Arg	Glu	Asp	Val	Thr	Leu	Lys	Glu	Leu	Met	Asp	Glu
				20					25					30
Glu	Asp	Val	Leu	Gln	Glu	Cys	Lys	Ala	Gln	Asn	Arg	Lys	Leu	Ile
				35					40					45
Glu	Phe	Leu	Leu	Lys	Ala	Glu	Cys	Leu	Glu	Asp	Leu	Val	Ser	Phe
				50					55					60
Ile	Ile	Glu	Glu	Pro	Pro	Gln	Asp	Met	Asp	Glu	Lys	Ile	Arg	Tyr
				65					70					75
Lys	Tyr	Pro	Asn	Ile	Ser	Cys	Glu	Leu	Leu	Thr	Ser	Asp	Val	Ser
				80					85					90
Gln	Met	Asn	Asp	Arg	Leu	Gly	Glu	Asp	Glu	Ser	Leu	Leu	Met	Lys
				95					100					105
Leu	Tyr	Ser	Phe	Leu	Leu	Asn	Asp	Ser	Pro	Leu	Asn	Pro	Leu	Leu
				110					115					120
Ala	Ser	Phe	Phe	Ser	Lys	Val	Leu	Ser	Ile	Leu	Ile	Ser	Arg	Lys
				125					130					135
Pro	Glu	Gln	Ile	Val	Asp	Phe	Leu	Lys	Lys	Lys	His	Asp	Phe	Val
				140					145					150
Asp	Leu	Ile	Ile	Lys	His	Ile	Gly	Thr	Ser	Ala	Ile	Met	Asp	Leu
				155					160					165
Leu	Leu	Arg	Leu	Leu	Thr	Cys	Ile	Glu	Pro	Pro	Gln	Pro	Arg	Gln
				170					175					180
Asp	Val	Leu	Asn	Trp	Leu	Asn	Glu	Glu	Lys	Ile	Ile	Gln	Arg	Leu
				185					190					195
Val	Glu	Ile	Val	His	Pro	Ser	Gln	Glu	Glu	Asp	Arg	His	Ser	Asn
				200					205					210
Ala	Ser	Gln	Ser	Leu	Cys	Glu	Ile	Val	Arg	Leu	Ser	Arg	Asp	Gln
				215					220					225
Met	Leu	Gln	Ile	Gln	Asn	Ser	Thr	Glu	Pro	Asp	Pro	Leu	Leu	Ala
				230					235					240
Thr	Leu	Glu	Lys	Gln	Glu	Ile	Ile	Glu	Gln	Leu	Leu	Ser	Asn	Ile
				245					250					255
Phe	His	Lys	Glu	Lys	Asn	Glu	Ser	Ala	Ile	Val	Ser	Ala	Ile	Gln
				260					265					270
Ile	Leu	Leu	Thr	Leu	Leu	Glu	Thr	Arg	Arg	Pro	Thr	Phe	Glu	Gly
				275					280					285
His	Ile	Glu	Ile	Cys	Pro	Pro	Gly	Met	Ser	His	Ser	Ala	Cys	Ser
				290					295					300
Val	Asn	Lys	Ser	Val	Leu	Glu	Ala	Ile	Arg	Gly	Arg	Leu	Gly	Ser
				305					310					315
Phe	His	Glu	Leu	Leu	Leu	Glu	Pro	Pro	Lys	Lys	Ser	Val	Met	Lys
				320					325					330
Thr	Thr	Trp	Gly	Val	Leu	Asp	Pro	Pro	Val	Gly	Asn	Thr	Arg	Leu
				335					340					345
Asn	Val	Ile	Arg	Leu	Ile	Ser	Ser	Leu	Leu	Gln	Thr	Asn	Thr	Ser
				350					355					360
Ser	Ile	Asn	Gly	Asp	Leu	Met	Glu	Leu	Asn	Ser	Ile	Gly	Val	Ile
				365					370					375
Leu	Asn	Met	Phe	Phe	Lys	Tyr	Thr	Trp	Asn	Asn	Phe	Leu	His	Thr
				380					385					390
Gln	Val	Glu	Ile	Cys	Ile	Ala	Leu	Ile	Leu	Ala	Ser	Pro	Phe	Glu
				395					400					405
Asn	Thr	Glu	Asn	Ala	Thr	Ile	Thr	Asp	Gln	Asp	Ser	Thr	Gly	Asp
				410					415					420
Asn	Leu	Leu	Leu	Lys	His	Leu	Phe	Gln	Lys	Cys	Gln	Leu	Ile	Glu
				425					430					435
Arg	Ile	Leu	Glu	Ala	Trp	Glu	Met	Asn	Glu	Lys	Lys	Gln	Ala	Glu
				440					445					450
Gly	Gly	Arg	Arg	His	Gly	Tyr	Met	Gly	His	Leu	Thr	Arg	Ile	Ala
				455					460					465
Asn	Cys	Ile	Val	His	Ser	Thr	Asp	Lys	Gly	Pro	Asn	Ser	Ala	Leu



Val	Gln	Gln	Leu	Ile	Lys	Asp	Leu	Pro	Asp	Glu	Val	Arg	Glu	Arg	470	475	480
Trp	Glu	Thr	Phe	Cys	Thr	Ser	Ser	Leu	Gly	Glu	Thr	Asn	Lys	Arg	485	490	495
Asn	Thr	Val	Asp	Leu	Met	Gln	Gln	Met	Thr	Ser	Asn	Phe	Ile	Asp	500	505	510
Gln	Phe	Gly	Phe	Asn	Asp	Glu	Lys	Phe	Ala	Asp	Gln	Asp	Asp	Ile	515	520	525
Gly	Asn	Val	Ser	Phe	Asp	Arg	Val	Ser	Asp	Ile	Asn	Phe	Thr	Leu	530	535	540
Asn	Thr	Asn	Glu	Ser	Gly	Asn	Ile	Ala	Leu	Phe	Glu	Ala	Cys	Cys	545	550	555
Lys	Glu	Arg	Ile	Gln	Gln	Phe	Asp	Asp	Gly	Gly	Ser	Asp	Glu	Glu	560	565	570
Asp	Ile	Trp	Glu	Glu	Lys	His	Ile	Ala	Phe	Thr	Pro	Glu	Ser	Gln	575	580	585
Arg	Arg	Ser	Ser	Ser	Gly	Ser	Thr	Asp	Ser	Glu	Glu	Ser	Thr	Asp	590	595	600
Ser	Glu	Glu	Glu	Asp	Gly	Ala	Lys	Gln	Asp	Leu	Phe	Glu	Pro	Ser	605	610	615
Ser	Ala	Asn	Thr	Glu	Asp	Lys	Met	Glu	Val	Asp	Leu	Ser	Glu	Pro	620	625	630
Pro	Asn	Trp	Ser	Ala	Asn	Phe	Asp	Val	Pro	Met	Glu	Thr	Thr	His	635	640	645
Gly	Ala	Pro	Leu	Asp	Ser	Val	Gly	Ser	Asp	Val	Trp	Ser	Thr	Glu	650	655	660
Glu	Pro	Met	Pro	Thr	Lys	Glu	Thr	Gly	Trp	Ala	Ser	Phe	Ser	Glu	665	670	675
Phe	Thr	Ser	Ser	Leu	Ser	Thr	Lys	Asp	Ser	Leu	Arg	Ser	Asn	Ser	680	685	690
Pro	Val	Glu	Met	Glu	Thr	Ser	Thr	Glu	Pro	Met	Asp	Pro	Leu	Thr	695	700	705
Pro	Ser	Ala	Ala	Ala	Leu	Ala	Val	Gln	Pro	Glu	Ala	Ala	Gly	Ser	710	715	720
Val	Ala	Met	Glu	Ala	Ser	Ser	Asp	Gly	Glu	Glu	Asp	Ala	Glu	Ser	725	730	735
Thr	Asp	Lys	Val	Thr	Glu	Thr	Val	Met	Asn	Gly	Gly	Met	Lys	Glu	740	745	750
Thr	Leu	Ser	Leu	Thr	Val	Asp	Ala	Lys	Thr	Glu	Thr	Ala	Val	Phe	755	760	765
Lys	Ser	Glu	Glu	Gly	Lys	Leu	Ser	Thr	Ser	Gln	Asp	Ala	Ala	Cys	770	775	780
Lys	Asp	Ala	Glu	Glu	Cys	Pro	Glu	Thr	Ala	Glu	Ala	Lys	Cys	Ala	785	790	795
Ala	Pro	Arg	Pro	Pro	Ser	Ser	Ser	Pro	Glu	Gln	Arg	Thr	Gly	Gln	800	805	810
Pro	Ser	Ala	Pro	Gly	Asp	Thr	Ser	Val	Asn	Gly	Pro	Val			815	820	825
				830					835								

&lt;210&gt; 45

&lt;211&gt; 408

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte ID No: 3044763CD1

&lt;400&gt; 45

Met	Arg	Thr	Asp	Ser	Gly	Ala	Arg	Leu	Glu	Glu	Gly	His	Leu	Arg
1				5				10					15	
Pro	Pro	Arg	Ala	Leu	Pro	Pro	Val	Pro	Ser	Gln	Asp	Asp	Ile	Pro

	20		25		30
Leu Ser Arg Pro Lys	Lys Lys Lys Pro Arg	Thr Lys Asn Thr Pro			
	35		40		45
Ala Ser Ala Ser Leu	Glu Gly Leu Ala Gln	Thr Ala Gly Arg Arg			
	50		55		60
Pro Ser Glu Gly Asn	Glu Pro Ser Thr Lys	Glu Leu Lys Glu His			
	65		70		75
Pro Glu Ala Pro Val	Gln Arg Arg Gln Lys	Lys Thr Arg Leu Pro			
	80		85		90
Leu Glu Leu Glu Thr	Ser Ser Thr Gln Lys	Lys Ser Ser Ser Ser			
	95		100		105
Ser Leu Leu Arg Asn	Glu Asn Gly Ile Asp	Ala Glu Pro Ala Glu			
	110		115		120
Glu Ala Val Ile Gln	Lys Pro Arg Arg Lys	Thr Lys Lys Thr Gln			
	125		130		135
Pro Ala Glu Leu Gln	Tyr Ala Asn Glu Leu	Gly Val Glu Asp Glu			
	140		145		150
Asp Ile Ile Thr Asp	Glu Gln Thr Thr Val	Glu Gln Gln Ser Val			
	155		160		165
Phe Thr Ala Pro Thr	Gly Ile Ser Gln Pro	Val Gly Lys Val Phe			
	170		175		180
Val Glu Lys Ser Arg	Phe Gln Ala Ala Asp	Arg Ser Glu Leu			
	185		190		195
Ile Lys Thr Thr Glu	Asn Ile Asp Val Ser	Met Asp Val Lys Pro			
	200		205		210
Ser Trp Thr Thr Arg	Asp Val Ala Leu Thr	Val His Arg Ala Phe			
	215		220		225
Arg Met Ile Gly Leu	Phe Ser His Gly Phe	Leu Ala Gly Cys Ala			
	230		235		240
Val Trp Asn Ile Val	Val Ile Tyr Val Leu	Ala Gly Asp Gln Leu			
	245		250		255
Ser Asn Leu Ser Asn	Leu Leu Gln Gln Tyr	Lys Thr Leu Ala Tyr			
	260		265		270
Pro Phe Gln Ser Leu	Leu Tyr Leu Leu Leu	Ala Leu Ser Thr Ile			
	275		280		285
Ser Ala Phe Asp Arg	Ile Asp Phe Ala Lys	Ile Ser Val Ala Ile			
	290		295		300
Arg Asn Phe Leu Ala	Leu Asp Pro Thr Ala	Leu Ala Ser Phe Leu			
	305		310		315
Tyr Phe Thr Ala Leu	Ile Leu Ser Leu Ser	Gln Gln Met Thr Ser			
	320		325		330
Asp Arg Ile His Leu	Tyr Thr Pro Ser Ser	Val Asn Gly Ser Leu			
	335		340		345
Trp Glu Ala Gly Ile	Glu Glu Gln Ile Leu	Gln Pro Trp Ile Val			
	350		355		360
Val Asn Leu Val Val	Ala Leu Leu Val Gly	Leu Ser Trp Leu Phe			
	365		370		375
Leu Ser Tyr Arg Pro	Gly Met Asp Leu Ser	Glu Glu Leu Met Phe			
	380		385		390
Ser Ser Glu Val Glu	Tyr Pro Asp Lys	Glu Lys Glu Ile Lys			
	395		400		405
Ala Ser Ser					

&lt;210&gt; 46

&lt;211&gt; 101

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte ID No: 4044519CD1

&lt;400&gt; 46

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Met Cys Phe Leu Phe Phe Leu Leu Phe Phe Thr Met Val Ala Ser
 1          5          10          15
Thr Cys Pro Ser Asp Leu Arg Leu Lys Asp Ser Phe Leu Lys Asn
          20          25          30
Met Val Pro Ala Leu Lys Gly Cys Phe Arg Thr Tyr Phe Ile Cys
          35          40          45
Phe Leu Leu Ile Leu Ile Phe Gln Leu Asn Pro Ser Ser Ser Leu
          50          55          60
Pro Ser Ser Leu Pro Val Tyr Leu Phe Ser Phe Leu Ser Phe Phe
          65          70          75
Phe Phe Phe Phe Phe Leu Glu Ala Glu Ser Cys Pro Val Thr Gln
          80          85          90
Ala Glu Val Gln Trp Tyr Asp His Ser Ser Leu
          95          100

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&lt;210&gt; 47

&lt;211&gt; 256

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte ID No: 71351918CD1

&lt;400&gt; 47

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Met Glu Asn Ser Gly Phe Phe Pro Ser Gly Leu Val Val Leu Ser
 1          5          10          15
Gly Gly Met Asp Ala Gln Leu Lys Ile Trp Ser Ala Glu Asp Ala
          20          25          30
Ser Cys Val Val Thr Phe Lys Gly His Lys Gly Gly Ile Leu Asp
          35          40          45
Thr Ala Ile Val Asp Arg Gly Arg Asn Val Val Ser Ala Ser Arg
          50          55          60
Asp Gly Thr Ala Arg Leu Trp Asp Cys Gly Arg Ser Gly Cys Leu
          65          70          75
Gly Val Leu Ala Asp Cys Gly Ser Ser Ile Asn Gly Val Ala Val
          80          85          90
Gly Ala Ala Asp Asn Ser Ile Asn Leu Gly Ser Pro Glu Gln Met
          95          100          105
Pro Ser Glu Arg Glu Val Gly Thr Glu Ala Lys Met Leu Leu Leu
          110          115          120
Ala Arg Glu Asp Lys Lys Leu Gln Cys Leu Gly Leu Gln Ser Arg
          125          130          135
Gln Leu Val Phe Leu Phe Ile Gly Ser Asp Ala Phe Asn Cys Cys
          140          145          150
Thr Phe Leu Ser Gly Phe Leu Leu Leu Ala Gly Thr Gln Asp Gly
          155          160          165
Asn Ile Tyr Gln Leu Asp Val Arg Ser Pro Arg Ala Pro Val Gln
          170          175          180
Val Ile His Arg Ser Gly Ala Pro Val Leu Ser Leu Leu Ser Val
          185          190          195
Arg Asp Gly Phe Ile Ala Ser Gln Gly Asp Gly Ser Cys Phe Ile
          200          205          210
Val Gln Gln Asp Leu Asp Tyr Val Thr Glu Leu Thr Gly Ala Asp
          215          220          225
Cys Asp Pro Val Tyr Lys Val Ala Thr Trp Glu Lys Gln Ile Tyr
          230          235          240
Thr Cys Cys Arg Asp Gly Leu Val Arg Arg Tyr Gln Leu Ser Asp
          245          250          255
Leu

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<210> 48  
 <211> 104  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte ID No: 8109363CD1

<400> 48  
 Met Pro Arg Ser Ser Gln His Ser Glu Ser Ser Pro Leu Asp Thr  
 1 5 10 15  
 Thr Thr Gln Arg Lys Gly Ala Ser Ser Leu Ala His Gln Val Arg  
 20 25 30  
 Val His Thr Leu Glu Thr Leu Leu Asp Trp Pro Glu Leu Pro Gln  
 35 40 45  
 Pro Leu Leu Thr Pro Pro Pro Val Ile Asp Thr Ala Ala Gly Ser  
 50 55 60  
 Arg Lys Arg Phe Leu Asn Lys Ala Gln Leu Ala Gln Cys Leu Ala  
 65 70 75  
 Gln Gln Thr Ile Asn Thr Cys Lys Leu Asn Cys Met Ile Leu Ala  
 80 85 90  
 Gln Val Leu Leu Met Trp Leu Thr Ala Thr His Leu His Gly  
 95 100

<210> 49  
 <211> 855  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte ID No: 1272746CD1

<400> 49  
 Met Ser Phe Val Arg Val Asn Arg Cys Gly Pro Arg Val Gly Val  
 1 5 10 15  
 Arg Lys Thr Pro Lys Val Lys Lys Lys Lys Thr Ser Val Lys Gln  
 20 25 30  
 Glu Trp Asp Asn Thr Val Thr Asp Leu Thr Val His Arg Ala Thr  
 35 40 45  
 Pro Glu Asp Leu Val Arg Arg His Glu Ile His Lys Ser Lys Asn  
 50 55 60  
 Arg Ala Leu Val His Trp Glu Leu Gln Glu Lys Ala Leu Lys Arg  
 65 70 75  
 Lys Trp Arg Lys Gln Lys Pro Glu Thr Leu Asn Leu Glu Lys Arg  
 80 85 90  
 Arg Leu Ser Ile Met Lys Glu Ile Leu Ser Asp Gln Tyr Gln Met  
 95 100 105  
 Gln Asp Val Leu Glu Lys Ser Asp His Leu Ile Ala Ala Ala Lys  
 110 115 120  
 Glu Leu Phe Pro Arg Arg Arg Thr Gly Phe Pro Asn Val Thr Val  
 125 130 135  
 Ala Pro Asp Ser Ser Gln Gly Pro Ile Val Val Asn Gln Asp Pro  
 140 145 150  
 Ile Thr Gln Ser Ile Phe Asn Glu Ser Val Ile Glu Pro Gln Ala  
 155 160 165  
 Leu Asn Asp Val Asp Gly Glu Glu Glu Gly Thr Val Asn Ser Gln  
 170 175 180  
 Ser Gly Glu Ser Glu Asn Glu Asn Glu Leu Asp Asn Ser Leu Asn  
 185 190 195  
 Ser Gln Ser Asn Thr Asn Thr Asp Arg Phe Leu Gln Gln Leu Thr  
 200 205 210

Glu	Glu	Asn	Phe	Glu	Leu	Ile	Ser	Lys	Leu	Trp	Thr	Asp	Ile	Gln
				215					220					225
Gln	Lys	Ile	Ala	Thr	Gln	Ser	Gln	Ile	Thr	Pro	Pro	Gly	Thr	Pro
				230					235					240
Ser	Ser	Ala	Leu	Ser	Ser	Gly	Glu	Gln	Arg	Ala	Ala	Leu	Asn	Ala
				245					250					255
Thr	Asn	Ala	Val	Lys	Arg	Leu	Gln	Thr	Arg	Leu	Gln	Pro	Glu	Glu
				260					265					270
Ser	Thr	Glu	Thr	Leu	Asp	Ser	Ser	Tyr	Val	Val	Gly	His	Val	Leu
				275					280					285
Asn	Ser	Arg	Lys	Gln	Lys	Gln	Leu	Leu	Asn	Lys	Val	Lys	Arg	Lys
				290					295					300
Pro	Asn	Leu	His	Ala	Leu	Ser	Lys	Pro	Lys	Lys	Asn	Ile	Ser	Ser
				305					310					315
Gly	Ser	Thr	Thr	Ser	Ala	Asp	Leu	Pro	Asn	Arg	Thr	Asn	Ser	Asn
				320					325					330
Leu	Asp	Val	Leu	Lys	His	Met	Ile	His	Glu	Val	Glu	His	Glu	Met
				335					340					345
Glu	Glu	Tyr	Glu	Arg	Trp	Thr	Gly	Arg	Glu	Val	Lys	Gly	Leu	Gln
				350					355					360
Ser	Ser	Gln	Gly	Leu	Thr	Gly	Phe	Thr	Leu	Ser	Leu	Val	Ser	Ser
				365					370					375
Leu	Cys	Arg	Leu	Val	Arg	Tyr	Leu	Lys	Glu	Ser	Glu	Ile	Gln	Leu
				380					385					390
Arg	Lys	Glu	Val	Glu	Thr	Arg	Gln	Gln	Leu	Glu	Gln	Val	Leu	Gly
				395					400					405
Asp	His	Arg	Glu	Leu	Ile	Asp	Ala	Leu	Thr	Ala	Glu	Ile	Leu	Arg
				410					415					420
Leu	Arg	Glu	Glu	Asn	Ala	Ala	Thr	Gln	Ala	Arg	Leu	Gln	Gln	Tyr
				425					430					435
Met	Val	Thr	Thr	Asp	Glu	Gln	Leu	Ile	Ser	Leu	Thr	His	Ala	Ile
				440					445					450
Lys	Asn	Cys	Pro	Val	Ile	Asn	Asn	Arg	Gln	Glu	Ile	Gln	Ala	Ser
				455					460					465
Glu	Ser	Gly	Ala	Thr	Gly	Arg	Arg	Val	Met	Asp	Ser	Pro	Glu	Arg
				470					475					480
Pro	Val	Val	Asn	Ala	Asn	Val	Ser	Val	Pro	Leu	Met	Phe	Arg	Glu
				485					490					495
Glu	Val	Ala	Glu	Phe	Pro	Gln	Glu	Glu	Leu	Pro	Val	Lys	Leu	Ser
				500					505					510
Gln	Val	Pro	Asp	Pro	Pro	Asp	Asn	Met	Asn	Leu	Ala	Lys	Asn	Phe
				515					520					525
Pro	Ala	His	Ile	Phe	Glu	Pro	Ala	Val	Leu	Leu	Thr	Pro	Pro	Arg
				530					535					540
Gln	Lys	Ser	Asn	Leu	Lys	Phe	Ser	Pro	Leu	Gln	Asp	Val	Leu	Arg
				545					550					555
Arg	Thr	Val	Gln	Thr	Arg	Pro	Ala	Pro	Arg	Leu	Pro	Pro	Thr	Val
				560					565					570
Glu	Ile	Ile	Glu	Lys	Glu	Gln	Asn	Trp	Glu	Glu	Lys	Thr	Leu	Pro
				575					580					585
Ile	Asp	Thr	Asp	Ile	Gln	Asn	Ser	Ser	Glu	Glu	Asn	Arg	Leu	Phe
				590					595					600
Thr	Gln	Arg	Trp	Arg	Val	Ser	His	Met	Gly	Glu	Asp	Leu	Glu	Asn
				605					610					615
Lys	Thr	Gln	Ala	Pro	Phe	Val	Asn	Leu	Ser	Gln	Pro	Leu	Cys	Asn
				620					625					630
Ser	His	Ser	Asn	Thr	Gln	Gln	Ser	Arg	Ser	Pro	Thr	Phe	Ser	Glu
				635					640					645
Glu	Leu	Pro	Val	Leu	Gly	Asp	Gly	Gln	Gln	Leu	Arg	Thr	Asn	Glu
				650					655					660
Ser	Leu	Ile	Gln	Arg	Lys	Asp	Ile	Met	Thr	Arg	Ile	Ala	Asp	Leu
				665					670					675
Thr	Leu	Gln	Asn	Ser	Ala	Ile	Lys	Ala	His	Met	Asn	Asn	Ile	Ile

	680		685		690
Glu Pro Arg Gly	Glu Gln Gly Asp Gly	Leu Arg Glu Leu Asn Lys			
	695		700		705
Gln Glu Ser Ala	Ser Asp Met Thr Ser	Thr Phe Pro Val Ala Gln			
	710		715		720
Ser Leu Thr Pro	Gly Ser Met Glu Glu	Arg Ile Ala Glu Leu Asn			
	725		730		735
Arg Gln Ser Met	Glu Ala Arg Gly Lys	Leu Leu Gln Leu Ile Glu			
	740		745		750
Gln Gln Lys Leu	Val Gly Leu Asn Leu	Ser Pro Pro Met Ser Pro			
	755		760		765
Val Gln Leu Pro	Leu Arg Ala Trp Thr	Glu Gly Ala Lys Arg Thr			
	770		775		780
Ile Glu Val Ser	Ile Pro Gly Ala Glu	Ala Pro Glu Ser Ser Lys			
	785		790		795
Cys Ser Thr Val	Ser Pro Val Ser Gly	Ile Asn Thr Arg Arg Ser			
	800		805		810
Ser Gly Ala Thr	Gly Asn Ser Cys Ser	Pro Leu Asn Ala Thr Ser			
	815		820		825
Gly Ser Gly Arg	Phe Thr Pro Leu Asn	Pro Arg Ala Lys Ile Glu			
	830		835		840
Lys Gln Asn Glu	Gly Trp Phe Ala	Leu Ser Thr His Val Ser			
	845		850		855

&lt;210&gt; 50

&lt;211&gt; 427

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte ID No: 1839974CD1

&lt;400&gt; 50

Met Tyr Val Thr Met	Met Met Thr Asp	Gln Ile Pro Leu Glu Leu			
1	5	10			15
Pro Pro Leu Leu Asn	Gly Glu Val Ala	Met Met Pro His Leu Val			
	20	25			30
Asn Gly Asp Ala Ala	Gln Gln Val Ile	Leu Val Gln Val Asn Pro			
	35	40			45
Gly Glu Thr Phe Thr	Ile Arg Ala Glu	Asp Gly Thr Leu Gln Cys			
	50	55			60
Ile Gln Gly Pro Ala	Glu Val Pro Met	Met Ser Pro Asn Gly Ser			
	65	70			75
Ile Pro Pro Ile His	Val Pro Pro Gly	Tyr Ile Ser Gln Val Ile			
	80	85			90
Glu Asp Ser Thr Gly	Val Arg Arg Val	Val Val Thr Pro Gln Ser			
	95	100			105
Pro Glu Cys Tyr Pro	Pro Ser Tyr Pro	Ser Ala Met Ser Pro Thr			
	110	115			120
His His Leu Pro Pro	Tyr Leu Thr His	His Pro His Phe Ile His			
	125	130			135
Asn Ser His Thr Ala	Tyr Tyr Pro Pro	Val Thr Gly Pro Gly Asp			
	140	145			150
Met Pro Pro Gln Phe	Phe Pro Gln His	His Leu Pro His Thr Ile			
	155	160			165
Tyr Gly Glu Gln Glu	Ile Ile Pro Phe	Tyr Gly Met Ser Thr Tyr			
	170	175			180
Ile Thr Arg Glu Asp	Gln Tyr Ser Lys	Pro Pro His Lys Lys Leu			
	185	190			195
Lys Asp Arg Gln Ile	Asp Arg Gln Asn	Arg Leu Asn Ser Pro Pro			
	200	205			210

Ser	Ser	Ile	Tyr	Lys	Ser	Ser	Cys	Thr	Thr	Val	Tyr	Asn	Gly	Tyr
				215					220					225
Gly	Lys	Gly	His	Ser	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Ser
				230					235					240
Gly	Pro	Gly	Ile	Lys	Lys	Thr	Glu	Arg	Arg	Ala	Arg	Ser	Ser	Pro
				245					250					255
Lys	Ser	Asn	Asp	Ser	Asp	Leu	Gln	Glu	Tyr	Glu	Leu	Glu	Val	Lys
				260					265					270
Arg	Val	Gln	Asp	Ile	Leu	Ser	Gly	Ile	Glu	Lys	Pro	Gln	Val	Ser
				275					280					285
Asn	Ile	Gln	Ala	Arg	Ala	Val	Val	Leu	Ser	Trp	Ala	Pro	Pro	Val
				290					295					300
Gly	Leu	Ser	Cys	Gly	Pro	His	Ser	Gly	Leu	Ser	Phe	Pro	Tyr	Ser
				305					310					315
Tyr	Glu	Val	Ala	Leu	Ser	Asp	Lys	Gly	Arg	Asp	Gly	Lys	Tyr	Lys
				320					325					330
Ile	Ile	Tyr	Ser	Gly	Glu	Glu	Leu	Glu	Cys	Asn	Leu	Lys	Asp	Leu
				335					340					345
Arg	Pro	Ala	Thr	Asp	Tyr	His	Val	Arg	Val	Tyr	Ala	Met	Tyr	Asn
				350					355					360
Ser	Val	Lys	Gly	Ser	Cys	Ser	Glu	Pro	Val	Ser	Phe	Thr	Thr	His
				365					370					375
Ser	Cys	Ala	Pro	Glu	Cys	Pro	Phe	Pro	Pro	Lys	Leu	Ala	His	Arg
				380					385					390
Ser	Lys	Ser	Ser	Leu	Thr	Leu	Gln	Trp	Lys	Ala	Pro	Ile	Asp	Asn
				395					400					405
Gly	Ser	Lys	Ile	Thr	Asn	Tyr	Leu	Leu	Glu	Trp	Asp	Glu	Val	Ser
				410					415					420
Leu	Phe	Ser	Tyr	Ser	Pro	Ile								
				425										

&lt;210&gt; 51

&lt;211&gt; 800

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte ID No: 1877336CD1

&lt;400&gt; 51

Met	Ala	Ala	Asn	Val	Gly	Asp	Gln	Arg	Ser	Thr	Asp	Trp	Ser	Ser
1				5					10					15
Gln	Tyr	Ser	Met	Val	Ala	Gly	Ala	Gly	Arg	Glu	Asn	Gly	Met	Glu
				20					25					30
Thr	Pro	Met	His	Glu	Asn	Pro	Glu	Trp	Glu	Lys	Ala	Arg	Gln	Ala
				35					40					45
Leu	Ala	Ser	Ile	Ser	Lys	Ser	Gly	Ala	Ala	Gly	Gly	Ser	Ala	Lys
				50					55					60
Ser	Ser	Ser	Asn	Gly	Pro	Val	Ala	Ser	Ala	Gln	Tyr	Val	Ser	Gln
				65					70					75
Ala	Glu	Ala	Ser	Ala	Leu	Gln	Gln	Gln	Gln	Tyr	Tyr	Gln	Trp	Tyr
				80					85					90
Gln	Gln	Tyr	Asn	Tyr	Ala	Tyr	Pro	Tyr	Ser	Tyr	Tyr	Tyr	Pro	Met
				95					100					105
Ser	Met	Tyr	Gln	Ser	Tyr	Gly	Ser	Pro	Ser	Gln	Tyr	Gly	Met	Ala
				110					115					120
Gly	Ser	Tyr	Gly	Ser	Ala	Thr	Pro	Gln	Gln	Pro	Ser	Ala	Pro	Gln
				125					130					135
His	Gln	Gly	Thr	Leu	Asn	Gln	Pro	Pro	Val	Pro	Gly	Met	Asp	Glu
				140					145					150
Ser	Met	Ser	Tyr	Gln	Ala	Pro	Pro	Gln	Gln	Leu	Pro	Ser	Ala	Gln
				155					160					165

Pro	Pro	Gln	Pro	Ser	Asn	Pro	Pro	His	Gly	Ala	His	Thr	Leu	Asn
				170					175					180
Ser	Gly	Pro	Gln	Pro	Gly	Thr	Ala	Pro	Ala	Thr	Gln	His	Ser	Gln
				185					190					195
Ala	Gly	Pro	Ala	Thr	Gly	Gln	Ala	Tyr	Gly	Pro	His	Thr	Tyr	Thr
				200					205					210
Glu	Pro	Ala	Lys	Pro	Lys	Lys	Gly	Gln	Gln	Leu	Trp	Asn	Arg	Met
				215					220					225
Lys	Pro	Ala	Pro	Gly	Thr	Gly	Gly	Leu	Lys	Phe	Asn	Ile	Gln	Lys
				230					235					240
Arg	Pro	Phe	Ala	Val	Thr	Thr	Gln	Ser	Phe	Gly	Ser	Asn	Ala	Glu
				245					250					255
Gly	Gln	His	Ser	Gly	Phe	Gly	Pro	Gln	Pro	Asn	Pro	Glu	Lys	Val
				260					265					270
Gln	Asn	His	Ser	Gly	Ser	Ser	Ala	Arg	Gly	Asn	Leu	Ser	Gly	Lys
				275					280					285
Pro	Asp	Asp	Trp	Pro	Gln	Asp	Met	Lys	Glu	Tyr	Val	Glu	Arg	Cys
				290					295					300
Phe	Thr	Ala	Cys	Glu	Ser	Glu	Glu	Asp	Lys	Asp	Arg	Thr	Glu	Lys
				305					310					315
Leu	Leu	Lys	Glu	Val	Leu	Gln	Ala	Arg	Leu	Gln	Asp	Gly	Ser	Ala
				320					325					330
Tyr	Thr	Ile	Asp	Trp	Ser	Arg	Glu	Pro	Leu	Pro	Gly	Leu	Thr	Arg
				335					340					345
Glu	Pro	Val	Ala	Glu	Ser	Pro	Lys	Lys	Lys	Arg	Trp	Glu	Ala	Ala
				350					355					360
Ser	Ser	Leu	His	Pro	Pro	Arg	Gly	Ala	Gly	Ser	Ala	Thr	Arg	Gly
				365					370					375
Gly	Gly	Ala	Pro	Ser	Gln	Arg	Gly	Thr	Pro	Gly	Ala	Gly	Gly	Ala
				380					385					390
Gly	Arg	Ala	Arg	Gly	Asn	Ser	Phe	Thr	Lys	Phe	Gly	Asn	Arg	Asn
				395					400					405
Val	Phe	Met	Lys	Asp	Asn	Ser	Ser	Ser	Ser	Ser	Thr	Asp	Ser	Arg
				410					415					420
Ser	Arg	Ser	Ser	Ser	Arg	Ser	Pro	Thr	Arg	His	Phe	Arg	Arg	Ser
				425					430					435
Asp	Ser	His	Ser	Asp	Ser	Asp	Ser	Ser	Tyr	Ser	Gly	Asn	Glu	Cys
				440					445					450
His	Pro	Val	Gly	Arg	Arg	Asn	Pro	Pro	Pro	Lys	Gly	Arg	Gly	Gly
				455					460					465
Arg	Gly	Ala	His	Met	Asp	Arg	Gly	Arg	Gly	Arg	Ala	Gln	Arg	Gly
				470					475					480
Lys	Arg	His	Asp	Leu	Ala	Pro	Thr	Lys	Arg	Ser	Arg	Lys	Lys	Met
				485					490					495
Ala	Ala	Leu	Glu	Cys	Glu	Asp	Pro	Glu	Arg	Glu	Leu	Lys	Lys	Gln
				500					505					510
Lys	Arg	Ala	Ala	Arg	Phe	Gln	His	Gly	His	Ser	Arg	Arg	Leu	Arg
				515					520					525
Leu	Glu	Pro	Leu	Val	Leu	Gln	Met	Ser	Ser	Leu	Glu	Ser	Ser	Gly
				530					535					540
Ala	Asp	Pro	Asp	Trp	Gln	Glu	Leu	Gln	Ile	Val	Gly	Thr	Cys	Pro
				545					550					555
Asp	Ile	Thr	Lys	His	Tyr	Leu	Arg	Leu	Thr	Cys	Ala	Pro	Asp	Pro
				560					565					570
Ser	Thr	Val	Arg	Pro	Val	Ala	Val	Leu	Lys	Lys	Ser	Leu	Cys	Met
				575					580					585
Val	Lys	Cys	His	Trp	Lys	Glu	Lys	Gln	Asp	Tyr	Ala	Phe	Ala	Cys
				590					595					600
Glu	Gln	Met	Lys	Ser	Ile	Arg	Gln	Asp	Leu	Thr	Val	Gln	Gly	Ile
				605					610					615
Arg	Thr	Glu	Phe	Thr	Val	Glu	Val	Tyr	Glu	Thr	His	Ala	Arg	Ile
				620					625					630
Ala	Leu	Glu	Lys	Gly	Asp	His	Glu	Glu	Phe	Asn	Gln	Cys	Gln	Thr



	635		640		645
Gln Leu Lys Ser	Leu Tyr Ala Glu Asn	Leu Pro Gly Asn Val	Gly		
	650		655		660
Glu Phe Thr Ala	Tyr Arg Ile Leu Tyr	Tyr Ile Phe Thr Lys	Asn		
	665		670		675
Ser Gly Asp Ile	Thr Thr Glu Leu Ala	Tyr Leu Thr Arg Glu	Leu		
	680		685		690
Lys Ala Asp Pro	Cys Val Ala His Ala	Leu Ala Leu Arg Thr	Ala		
	695		700		705
Trp Ala Leu Gly	Asn Tyr His Arg Phe	Phe Arg Leu Tyr Cys	His		
	710		715		720
Ala Pro Cys Met	Ser Gly Tyr Leu Val	Asp Lys Phe Ala Asp	Arg		
	725		730		735
Glu Arg Lys Val	Ala Leu Lys Ala Met	Ile Lys Thr Phe Arg	Pro		
	740		745		750
Ala Leu Pro Val	Ser Tyr Leu Gln Ala	Glu Leu Ala Phe Glu	Gly		
	755		760		765
Glu Ala Ala Cys	Arg Ala Phe Leu Glu	Pro Leu Gly Leu Ala	Tyr		
	770		775		780
Thr Gly Pro Asp	Asn Ser Ser Ile Asp	Cys Arg Leu Ser Leu	Ala		
	785		790		795
Gln Leu Ser Ala	Phe				
	800				

<210> 52  
 <211> 107  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte ID No: 2321054CD1

<400> 52	
Met Ala Gly Gly Tyr Gly Val Met Gly Asp Asp Gly Ser Ile Asp	
1 5 10 15	
Tyr Thr Val His Glu Ala Trp Asn Glu Ala Thr Asn Val Tyr Leu	
20 25 30	
Ile Val Ile Leu Val Ser Phe Gly Leu Phe Met Tyr Ala Lys Arg	
35 40 45	
Asn Lys Arg Arg Ile Met Arg Ile Phe Ser Val Pro Pro Thr Glu	
50 55 60	
Glu Thr Leu Ser Glu Pro Asn Phe Tyr Asp Thr Ile Ser Lys Ile	
65 70 75	
Arg Leu Arg Gln Gln Leu Glu Met Tyr Ser Ile Ser Arg Lys Tyr	
80 85 90	
Asp Tyr Gln Gln Pro Gln Asn Gln Ala Asp Ser Val Gln Leu Ser	
95 100 105	
Leu Glu	

<210> 53  
 <211> 522  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte ID No: 2796034CD1

<400> 53	
Met Thr Pro Gly Lys His Ser Gly Ala Ser Ala Arg Ala Ala Asn	
1 5 10 15	

Ala	Gly	Ala	Trp	Gly	Tyr	Arg	Asp	Phe	Arg	Gly	Gly	Gln	Lys	Lys
				20					25					30
Gly	Trp	Cys	Thr	Thr	Pro	Gln	Leu	Val	Ala	Thr	Met	Pro	Val	Ser
				35					40					45
Pro	Ala	Gly	Ser	His	Lys	Gln	Gln	Asn	Phe	Gly	Leu	Asn	Asn	Ala
				50					55					60
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&lt;211&gt; 1992

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

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&lt;223&gt; Incyte ID No: 7494391CB1

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&lt;221&gt; unsure

&lt;222&gt; 1962

&lt;223&gt; a, t, c, g, or other

&lt;400&gt; 60

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<212> DNA

<213> Homo sapiens

<220>

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<223> Incyte ID No: 6451054CB1

<400> 61

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&lt;211&gt; 3236

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte ID No: 7494592CB1

&lt;220&gt;

&lt;221&gt; unsure

&lt;222&gt; 3215

&lt;223&gt; a, t, c, g, or other

&lt;400&gt; 62

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&lt;210&gt; 63

&lt;211&gt; 1906

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&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte ID No: 2013529CB1

&lt;400&gt; 64

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&lt;220&gt;

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&lt;223&gt; Incyte ID No: 8068623CB1

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&lt;211&gt; 2329

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&lt;213&gt; Homo sapiens

&lt;220&gt;

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&lt;223&gt; Incyte ID No: 677977CB1

&lt;400&gt; 70

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&lt;211&gt; 2960

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte ID No: 1661472CB1

&lt;400&gt; 71

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&lt;400&gt; 72

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&lt;213&gt; Homo sapiens

&lt;220&gt;

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&lt;223&gt; Incyte ID No: 2159545CB1

&lt;400&gt; 73

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&lt;223&gt; Incyte ID No: 8560269CB1

&lt;400&gt; 74

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&lt;223&gt; Incyte ID No: 2804937CB1

&lt;400&gt; 78

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 <213> Homo sapiens

<220>  
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 <223> Incyte ID No: 2073751CB1

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&lt;211&gt; 2691

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&lt;223&gt; Incyte ID No: 3178841CB1

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&lt;220&gt;

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&lt;223&gt; Incyte ID No: 3674807CB1

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&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte ID No: 1794922CB1

&lt;400&gt; 83

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&lt;220&gt;

&lt;221&gt; misc\_feature

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&lt;213&gt; Homo sapiens

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&lt;223&gt; Incyte ID No: 219442CB1

&lt;400&gt; 86

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&lt;223&gt; Incyte ID No: 168571CB1

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&lt;211&gt; 3621

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

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&lt;223&gt; Incyte ID No: 8227004CB1

&lt;400&gt; 100

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&lt;211&gt; 2704

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&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte ID No: 3044763CB1

&lt;400&gt; 101

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&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte ID No: 4044519CB1

&lt;400&gt; 102

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&lt;210&gt; 103

&lt;211&gt; 1607

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

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&lt;223&gt; Incyte ID No: 71351918CB1

&lt;400&gt; 103

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&lt;210&gt; 104

&lt;211&gt; 2622

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte ID No: 8109363CB1

&lt;400&gt; 104

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&lt;211&gt; 3489

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&lt;213&gt; Homo sapiens

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&lt;223&gt; Incyte ID No: 1272746CB1

&lt;400&gt; 105

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&lt;210&gt; 106

&lt;211&gt; 2269

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte ID No: 1839974CB1

&lt;400&gt; 106

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&lt;210&gt; 107

&lt;211&gt; 3075

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte ID No: 1877336CB1

&lt;400&gt; 107

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&lt;210&gt; 108

&lt;211&gt; 849

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte ID No: 2321054CB1

&lt;400&gt; 108

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&lt;211&gt; 2659

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte ID No: 2796034CB1

&lt;400&gt; 109

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&lt;210&gt; 110

&lt;211&gt; 2205

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte ID No: 4413112CB1

&lt;400&gt; 110

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